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WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

WINTER 1987

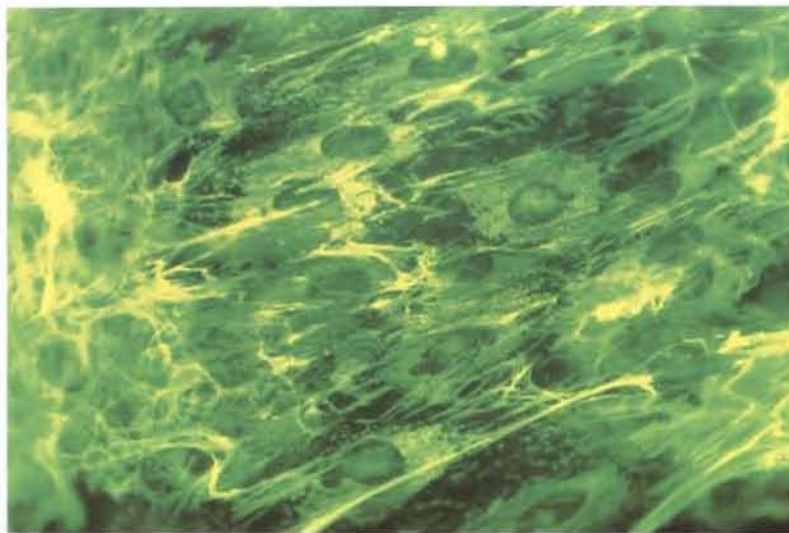
OUTLOOK

MAGAZINE

v. 24 n. 4, WIK 1987

A close-up portrait of a woman with dark skin and hair, smiling warmly at the camera. She has a small, ornate nose ring in her left nostril and a thin hoop earring in her right ear. She is wearing a green, textured shawl or wrap around her shoulders. Her hands are visible in the foreground, holding a lit cigarette. The background is a clear, bright blue sky.

Medicine in the
Third World



Fibronectin (above) is one of several connective tissue proteins known to play a major role in tissue architecture, development, wound healing and disease. See story on page 12.

OUTLOOK

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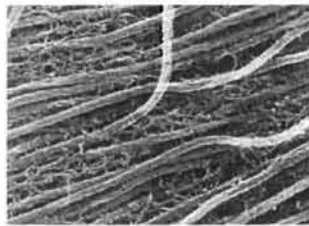
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School of Medicine



Healing the Silent Epidemic

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The Head Injury Resource Center helps head trauma patients lead productive, fulfilling lives.

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Connective tissue research becomes a hot topic as more is learned about the role of connective tissue proteins in tissue architecture, development, wound healing and disease.

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On the Cover:

Photo by Charles Miller, M.D., shows an Indian peddler holding a cigarette in the end of her fist.

Miller, who has practiced medicine in the third world, explains that Indian natives believe that smoking is not harmful if the smoke is inhaled through the hand, instead of directly from the end of the cigarette.

NEWSBRIEFS

School of Medicine Celebrates NIH's 100th Anniversary

For the National Institutes of Health to survive, it must change and develop emergency mechanisms to handle situations such as the AIDS crisis.

That was just one of the ideas presented last October at a symposium to commemorate the centennial of the National Institutes of Health (NIH). The symposium in Moore Auditorium at the School of Medicine brought together Nobel Prize winners, congressmen, NIH officials and School of Medicine faculty and staff to celebrate 100 years of accomplishment and take a long, hard look into the future.

During the morning program, Nobel Prize-winning researchers—each of whom conducted investigations with funding from the NIH—discussed their work. Arthur Kornberg, M.D., who was a microbiology professor at Washington University from 1953 to 1959 and is now professor of biochemistry at Stanford University School of Medicine, discussed his research on enzyme replication. Michael S. Brown, M.D., Paul J. Thomas Professor of Genetics in molecular genetics at the University of Texas Health Science Center in Dallas, talked about his studies with Lovastatin to lower cholesterol levels. Eye, brain and perception was the topic for David H. Hubel, M.D., the John F. Enders Professor in neurobiology at Harvard Medical School.

"The way things are" clashed with "the way things should be" at the afternoon panel discussion.

Everyone agreed that continued government funding is vital to the future of biomedical research. Panelists Samuel O. Thier, M.D., president of the Institute of Medicine of the National Academy of Sciences, and U.S. Representative Doug Walgren of Pennsylvania, chairman of the House subcommittee on science, research and technology, were optimistic and spoke of the need to rally public support behind federal funding for biomedical research.

But former Senator Thomas F. Eagleton warned that, due to economic and political considerations, the NIH will have to tighten its belt and put some of its programs on hold. "Everyone here would like zillions in government funds for research, education, and all of those good and noble things," said Eagleton, University Professor of Public Affairs at Washington University. "But we no longer have zillions."

"Like it or not, the NIH will have to take a hit and figure out how to reduce its research on a year by year basis throughout whatever depression or recession we're in, and then hope for a better day. When the crash comes, it hits everyone."

Carol Scheman, who lobbies on behalf of research universities for the Associa-



Drs. David M. Kipnis and Samuel O. Thier discuss issues of funding for medical research.

tion of American Universities, spoke of the need to strike a balance between health and other urgent priorities now facing the nation. "When I go to Capitol Hill to plead for more funds, it's as if I'm asking senators, congressmen and their staffs to cut internal infant health programs, cut farm programs and cut low income energy maintenance programs. That's the truth we're dealing with now."

The NIH budget was \$6.2 billion in 1987, a 17 percent increase over 1986, Scheman said. But Scheman agreed with Eagleton that the days of no-holds-barred government spending are numbered, that future funds will be scaled back, and that the public and

its legislators will face difficult and painful choices about where the money should go.

David M. Kipnis, M.D., professor of medicine and chairman of the Department of Internal Medicine at Washington University, lauded the Monsanto Company's contribution to and interaction with the school. He called for increased support to research universities from corporations and industry.

"Corporations as a collective group give remarkably little support to academic institutions," Kipnis said. "Less than 3 percent of the total basic science budget in the U.S. is supported by corporate activity. We need to recognize that all segments of society have a significant role

to play, and all segments can make a positive contribution."

William Raub, associate director of the NIH, cautioned the panel that politicians and the taxpayers who vote them into office tend to support short-term, practical results instead of basic science for its own sake. Researchers, on the other hand, know the importance of basic science and often cannot believe that its benefits are not immediately obvious to everyone else. "Since the post-World War II era, we've been driven by this utilitarian point of view," said Raub. He stressed the need to develop criteria by which to explain and defend biomedical research to the public.

Most panel members were dismayed that political considerations so often seem to outweigh what is best for society as a whole. Virginia Weldon, M.D., deputy vice chancellor for medical affairs at Washington University, suggested the need to re-evaluate earlier values and goals and to develop new ones.

"We've built a system for biomedical research and education that's unparalleled in human history," said Weldon. "This system has improved the health of mankind and shaped the world in which we live.

"Today," Weldon continued, "you've heard evidence that this world is now changing, and we've described these changes—some of them threats, some of them opportunities. I think we should be aware of the threats, analyze the existing system to look for its strengths and view the changes as opportunities." ■

New AIDS Clinical Studies Center Begins Testing of New Drugs and Promising Therapies

The School of Medicine recently began drug-test protocols in its new capacity as a designated AIDS Clinical Studies Group.

Washington University was one of 17 such study groups selected for funding by the National Institutes of Health. As such, the School of Medicine will receive \$5.5 million over five years to develop better AIDS treatment methods, conduct basic and clinical research and improve public and physician education.

The new centers will together receive a total of \$100 million from the National Institute of Allergy and Infectious Diseases to extend the clinical testing of promising AIDS therapies to many patients in a much wider geographic area than was previously possible. In addition, physicians near these new centers will now have access to experienced clinicians who are actively involved in AIDS patient care, in AIDS basic research and in the evaluation of new AIDS treatments.

At least 20 Washington University physicians and researchers will participate in the new center. It will include a set of core laboratories offering the latest diagnostic and prognostic techniques in the evaluation of AIDS patients.

The number of AIDS patients in the St. Louis area alone is expected to rise to somewhere between 2,000

and 4,000 by 1991, according to the new center's co-principal investigator Lee Ratner, M.D., Ph.D., assistant professor of medicine. Ratner is a leading AIDS researcher whose experiments with AIDS virus DNA have shown which of the virus' genes are involved in infecting and killing human immune system cells.

"AIDS is no longer just a problem of the East and West Coasts," Ratner says. "Although the prevalence is lower in the Midwest, AIDS is definitely a serious problem here. There are enough cases now that we can do clinical studies of almost equal magnitude to those in other cities and study promising drugs as part of the national effort."

Research at the center will draw upon the faculty's expertise in a variety of disciplines, among them cell and molecular biology, immunology, virology and neurology. These researchers will work to learn more about the function of immune system cells, develop more accurate methods for estimating the amount of AIDS virus in tissues, find out how AIDS affects the nervous system, compare the effectiveness of new and old drugs and discover better treatments for cryptococcal meningitis, a fungal infection that afflicts many AIDS patients.

In addition to patient care and research, the new center will promote physician and

public education by assisting existing agencies in public outreach programs, sponsoring special continuing education courses for healthcare professionals and serving as a regional resource for information on AIDS.

"The new center will combine the testing of new drugs for the treatment of AIDS with research efforts and an educational outreach program," says Gerald Medoff, M.D., a professor of medicine and of microbiology and immunology who is the center's other co-principal investigator. "Our efforts will be to provide the best and most up-to-date treatment for patients with AIDS, to develop new forms of therapy and to educate physicians in the surrounding community so that they can better care for their own patients." Medoff is an infectious diseases specialist who is expert in the diagnosis and treatment of the fungal and bacterial infections that are common in AIDS patients.

Patients and physicians seeking information or medical consultations from the staff of the Washington University study group are invited to use a special phone line established by the center. The number is 314-454-0058, and the hours of the phone service are 9 a.m. to 5 p.m., Monday through Friday. ■



Employees of the School of Medicine are encouraged to take advantage of a new day care center, sponsored jointly by the School of Medicine and Children's Hospital. For more information on the Child Development Center, located at 5457 Highland Park Drive, call the office of Robert J. Hickok at 362-6823, or the center at 533-6737.

Early Transplant Rejection Detected with Radioactively Labeled White Blood Cells

Transplant rejection can be detected non-invasively and with great sensitivity, using a new method that traces radioactively-labeled lymphocytes—a class of white blood cells—as they invade and accumulate in transplanted organs.

The infiltration of transplanted organs by the body's protective white blood cells is one of the most pronounced features of early rejection, according to researchers at the School of Medicine. It is this very feature that enables them to detect heart transplant rejection in experimental animals by injecting them with radioactively-tagged white blood cells and measuring the ensuing radiation levels in the transplanted organs.

Their new white blood cell method not only correlated well with results from conventional biopsy, but also detected rejection early enough for anti-rejection therapy to be effective. Having attained such promising results in animals, the Washington University team led by Steven R. Bergmann, M.D., Ph.D., assistant professor of medicine, in collaboration with R. Morton Bolman III, M.D., associate professor of surgery, is gearing up to begin similar studies in humans.

In contrast with conventional biopsy, which entails the removal of sample tissue from the transplanted organ,

the new white blood cell method requires the simple withdrawal and return of some white blood cells.

The method may even be more accurate than biopsy in some cases, according to Bergman. If rejection is patchy, for instance, it may go undetected when the biopsied tissue is not from a region in the organ where rejection is taking place. A gamma camera, on the other hand, is capable of screening the entire organ for infiltration of the radiolabeled lymphocytes.

While the new procedure promises to become an effective adjunct to biopsy, it is not likely to replace tissue sampling entirely, because of problems associated with repeated exposure to radiation. Heart transplant patients are typically tested for rejection on a weekly basis, which is too frequent to use the imaging technique. The new method will more likely serve as a "second opinion" in the case of sketchy or otherwise questionable biopsy results.

Better detection of organ rejection is vitally important to an estimated 1,400 new heart transplant patients each year, of whom 20 to 60 percent will require some type of therapy for acute episodes of rejection. ■

Two Alumni Faculty Members Awarded MERITs

Two alumni faculty members have been awarded MERIT—Method to Extend Research in Time—status for their recent grants, placing the total number of School of Medicine faculty members to receive MERIT awards at eight.

John O. Holloszy, M.D., professor of internal medicine and director of the applied physiology section in the Department of Internal Medicine, was granted \$726,243 from the National Institute on Aging, part of the National Institutes of Health (NIH).

A 1957 graduate of the School of Medicine, Holloszy's research has provided information regarding the biochemical basis for the increase in muscular endurance that occurs in response to exercise training,

and has provided new insights into the role of exercise in the maintenance of health and treatment of a number of degenerative diseases of middle and old age, including ischemic heart disease, type II diabetes and high blood pressure. He is currently trying to determine the role of physical inactivity in the deterioration of functional capacity associated with aging, and the reversibility of these changes by means of exercise training.

M. Alan Permutt, M.D., professor of medicine, was granted \$995,361 from the NIH's National Institute of Diabetes and Digestive and Kidney Diseases to find genetic markers that predict who is at high risk for developing diabetes.

Permutt has already identified one genetic marker for the disease, and has made important strides in discovering others. In trying to pinpoint which genes predispose people to diabetes, he is studying cloned insulin genes as well as the genes that regulate them. In 1983, he and his



M. Alan Permutt, M.D.

colleagues were the first to identify a specific gene marker for non-insulin dependent diabetes, the milder, most common form of the disease.

A 1965 graduate of the School of Medicine, Permutt directs the Institutional National Service Research Training Program in Endocrinology and Metabolism and is a former director of the Diabetes Clinic. ■

Outlook Rated Number One

The School of Medicine was honored last November by the Association of American Medical Colleges Group on Public Affairs for producing the best external periodical of any medical school or hospital in the nation.

Outlook was judged best for "outstanding layout and illustration, with imaginative writing making every topic interesting" in an annual competition that brought in a record 140 entries from medical schools, teaching hospitals and academic medical centers from across the country.

The Association of American Medical Colleges represents all 127 U.S. medical schools, more than 400 teaching hospitals, more than 70 medical societies and all medical students. ■



John O. Holloszy, M.D.

New Program for Graduates of the Medical Scientist Training Program

The School of Medicine will start accepting applications for a new Post-Graduate Medical Scientist Training Program (PGMSTP) this July.

A continuation of the Medical Scientist Training Program (MSTP), the new program was designed to guide talented M.D./Ph.D. graduates through their clinical

training, while providing them with continued access to the latest scientific developments in the physical and biological sciences. A two-year post-graduate research experience will be offered to all candidates of the new program, so that they may acquire whatever skills and interactions they need to pursue areas they will focus on

during their early academic careers.

In keeping with the interdepartmental nature of all graduate programs at Washington University, members of the PGMSTP will have access to any laboratory within the university, including those in the Monsanto Company which jointly sponsors a program in biotechnology. ■

It was the summer of 1971. Mark Weber, a 16-year-old from DeSoto, Missouri, had just completed his junior year in high school. With an academic honors background, he was beginning to think of following both his parents' footsteps into an education career. He would attend the University of Missouri at Columbia and become a teacher. But first there was high school to finish and the baseball and track events that filled his after-school hours.

On July 10, 1971, Weber was driving his family's 1970 Volkswagen van along a backroad near Cedar Hill, Missouri, when the van and an oncoming car collided head-on.

Weber was thrown through the windshield into a cornfield. Though he still carries marks on his body from the sheared cornstalks, those cosmetic scars seem minor compared to the severe head injury he sustained—a physical impairment that is invisible to the public eye, but with which Weber must struggle each day.

"The Silent Epidemic" is the term that has been coined by the National Head Injury Foundation, Inc., (NHIF) to describe the changes in emotions, thought processes and physical disabilities experienced by 50,000 to 70,000 head injury victims each year.

Most people who sustain head injuries are under the age of 30, according to the NHIF, and are injured in motor vehicle or sports accidents. Until recent years, many of these people were institutionalized in psychiatric hospitals, schools for the retarded or nursing homes.

Others such as Weber, who appear to recover, are given little help in the way of coping with their problems.

"If you met most of these people on the street, you probably wouldn't notice any deficit," says Bruce Crosson, Ph.D., a neuropsychologist and director of the Head Injury Resource Center (HIRC) of the Irene Walter Johnson Rehabilitation Institute at Washington University Medical Center.

The HIRC was established in 1985 to address the unique rehabilitation needs of

Patients at the Head Injury Resource Center develop independence by planning, organizing and carrying out normal, everyday activities such as preparing a meal. In this exercise, Mark Weber selects a menu, makes a shopping list, purchases the food and cooks a meal.



Healing The Silent



Silent Epidemic

By Brenda Murphy



Occupational therapist Peggy Barco encourages Mark to pay attention to and take notes about his surroundings, two strategies that make it easier for him to find his way to and from the campus bookstore.

patients who have suffered brain damage from head injuries or related injuries and diseases. It accepted its first patients in the spring of 1986, and began its Comprehensive Day Treatment Program in June 1986.

Crosson says that rehabilitative treatment of the head injured is becoming more prevalent due to the advocacy work of the NHIF, which was founded in 1980, and to the fact that more people are surviving traumatic head injuries.

"There are more survivors of traumatic head injuries due to advances in emergency medical care and the sophistication of technology in diagnosing and treating head injuries," Crosson says.

Crosson and his staff provide individualized therapy for these survivors of head injury, as well as for people with other forms of brain injury or disease such as cerebral anoxia, stroke or tumor.

But because treatment focuses on the long-term problems of brain injury that are likely to affect patients for the rest of their lives, patients generally do not enter the program until several months or more after injury. By that time, Crosson explains, the rapid recovery they experience during the first few months has leveled off, and it's easier to tell what the long-term deficits will be.

These long-term deficits often include personality changes, emotional changes, cognitive changes and physical changes.

Personality and cognitive changes occur in about 60 percent of head injury patients, according to Crosson. "Studies have shown that these mental changes are as or more disabling than physical disabilities in 72 percent of patients," he says.

Commonly seen cognitive changes include a loss of motivation to participate in productive activities and difficulty in forming new memories, organizing and planning activities, focusing attention on important information and solving complex problems.

Emotional changes span the gamut from displaying no emotion to experiencing intensified emotional reactions, such as outbursts of anger. Physical changes can include a loss of strength, difficulty in controlling body movements and decreased coordination or balance.

Both members of the patient population and their families must make psychological adjustments to the head injury, according to Crosson. He cites the case of a medical student who suffers a head injury: "He can't handle medical school anymore, and someone in rehabilitation is saying, 'You can file papers now.'"

"Sometimes the family can't cope with the loss," Crosson says, "although there are many more examples of families providing great emotional support. Patients more typically experience the loss of previous friendships and participation in social events."

The HIRC program involves both patients and families. Clients in the Comprehensive Day Treatment Program attend the program for six hours a day, four days a week, for four to six months. Two-month extensions are available. Parents or other designated family members attend family group sessions every other Wednesday. (A less intensive treatment program also is available.)

The HIRC therapy team includes: neuropsychologists, occupational therapists, a physical therapist and a speech and language pathologist.

Working Hard to Get Back to Work

When asked to name the favorite part of his job, Lou Combrevis, a 28-year-old material handler at McDonnell Douglas Astronautics Company and recent graduate of the Head Injury Resource Center (HIRC) at the Irene Walter Johnson Rehabilitation Institute, is quick to reply.

"Fridays," he says, smiling. "The thing that makes me happiest out there is Fridays because it's payday."

Lou Combrevis' answer is one shared by many workers. But if the truth be known, according to his parents, returning to work meant much more to Lou than just earning a paycheck. It was the driving force that helped him come back from a car accident that caused severe head injuries resulting in a coma and a four-month hospital stay.

Although Lou can't actually remember the accident, he relays what's been told to him as his parents, Leonard and Veronica Combrevis, listen in their South St. Louis County home.

On April 29, 1986, Lou was driving southbound on Interstate 270. Between Interstate 44 and Gravois, an 18-wheeler that had been off the side of the highway pulled in front of Lou's car.

"I swerved right to miss it," says Lou, speaking slowly, his speech still impaired from the accident. "But I caught his back end."

Details of the accident are sketchy, according to Leonard Combrevis, who says it looked as though Lou's car had been caught up underneath the 18-wheeler. The roof had been pushed in on the car. A paramedic, who passed by the accident, kept Lou alive until an ambulance arrived on the scene.

Lou was taken to St. Anthony's Medical Center in South St. Louis County, where he remained in a coma for a month. He was transferred to St. John's Mercy Medical Center in West St. Louis County, where he was hospitalized in a semi-conscious state for another three months and received intensive rehabilitation.

It was a speech pathologist at St. John's who recommended the HIRC rehabilitation program. Lou entered the program on Dec. 1, 1986, and remained for eight months.

The most helpful part of the program, Lou says, was "talking to the other people there. Then I'd come home and practice the things I needed to work on."

Those "things," according to Lou, included "a little bit of everything" from reading and writing to multiplication. Lou took his work at the HIRC quite seriously.

"They were surprised I did more homework than they wanted me to," Lou says, looking in the direction of his parents.

"He'd get that book and he'd work at it," says Leonard Combrevis. "We told him it wouldn't be easy. It would be a hard road."

Adds Veronica Combrevis: "He's really worked hard and he's got a good attitude about it."

The Combrevises give HIRC a great deal of credit for Lou's improvement. "I think the program is good," says Leonard Combrevis. "The alternative is to do nothing. We'd be lost in knowing how to help him. I don't know how we'd have gotten him to this point without the program. We'd help him in any way we could."

Adds Veronica Combrevis: "We tell him he's a lucky boy to be alive. We had to train him to do everything."

Lou graduated from the HIRC program in July and returned to work in late August with the assistance of the Missouri Division of Vocational Rehabilitation Services. He's being slowly retrained in his old job. "The more I do out there, the quicker it comes back," Lou says.

"At McDonnell Douglas, everybody has been tremendous," says Leonard Combrevis, who also worked for the company until he retired last spring. "They wanted him back. They're bringing him on slowly and working him back into his old position. His immediate boss says he's doing a real good job for him."

Lou works from 6:30 a.m. to 3 p.m. Mondays through Fridays, riding to work with friends. His parents are in the process of teaching him to drive again. He bowls, plays golf, dances and is looking forward to the day he can return to playing shortstop on a company softball team.

Lou seems genuinely proud of his accomplishments, such as recently earning his five-year employee pin at McDonnell Douglas and the amount of homework he did while enrolled at HIRC.

"When you get done out there (during the day program at HIRC), don't think it's over," Lou advises. "Go home and get ready for the next day. . . They told me nobody did as much as I did out there."

But then Lou had a reason to work hard.

"I wanted to get back to work," he says. "I just wanted to work hard to get back to work." ■



Lou Combrevis is back on the job at McDonnell Douglas.



(Inset photo): Posing as a customer, vocational rehabilitation counselor Diane Werts helps Mark improve his accuracy, speed and overall efficiency at making change. This particular exercise is of great practical value in Mark's part-time job at a gas station.

"We think more in terms of compensation rather than trying to get back a function," explains Crosson. "We try to improve the ability of the person as much as we can. Some deficits have been there for a long period of time. We show them ways to get around it."

Sessions include: cognitive retraining to build speed and efficiency in processing information and specialized therapy to treat individual speech and language deficits, physical coordination problems, psychological needs and career counseling. An adjustment group helps patients become aware and accept problem areas, and job trials within the medical center complex increase their ability to function in the community.

Mark Weber entered the HIRC program in September—16 years after his accident.

Although he appeared to have physically recovered from the head injury—which left him in a coma for two weeks, paralyzed on his left side for nearly a month and hospitalized for 10 weeks at Barnes Hospital—he was left with daily struggles in performing such common tasks as grocery shopping or following directions.

Academics, which had come easily to him before the accident, now presented real problems.

"I would study for hours on end before a test, then go to sleep. I'd wake up the next morning thinking I was all ready for

the test and all the information would be gone," recalls Weber, who graduated from DeSoto High School in 1972 with the aid of a tutor.

"I revised my educational goals," says Weber, who enrolled in a local community college instead of attending the University of Missouri at Columbia.

He became interested in pursuing a career in physical therapy, influenced by his own hospital experience. But when it came to memorizing the long lists of body parts required in his anatomy and physiology courses, Weber became discouraged. He dropped out of school after one-and-a-half years and joined the Army.

He studied to become a combat medic at the Army's Academy of Health Sciences at Fort Sam Houston, Texas. "I was able to struggle through. I wasn't at the top of my class," Weber recalls.

He served as an Army medic from 1974 through 1981, stationed at hospitals in Colorado, West Germany and Hawaii, earning the rank of sergeant.

"I progressed through the ranks pretty quickly," Weber says. "It was noted on my reports most often that I was absent-minded or forgetful. That was attributed to me as a character fault. I feel I did well in the military because it's a fairly structured lifestyle. One day is like another. You follow a certain routine."

He left active duty in 1981 and began to pursue a degree in nursing, first at Deaconess College of Nursing in St. Louis and later at Jewish Hospital School of Nursing.

Difficulties in keeping up with his studies forced Weber to drop out of nursing school. He married a fellow nursing student and began working in her father's service station in downtown St. Louis. Even working in the gas station proved difficult.

It was Weber's wife, Gloria, who began to notice his memory problems. The couple has an 18-month-old daughter, and Mrs. Weber often sends her husband to the grocery store to pick up a few items. "A list of 10 items would take me one and a-half hours to get," Weber says.

Weber also began to notice difficulty with his sense of direction. When told he could find his shirt in the bedroom, he would make the wrong turn in the house to get there. He'd also turn in the wrong direction when driving to a familiar location.

"My wife and in-laws said I had a problem. I knew myself I had a problem

with my memory after my frustrating efforts to get into nursing," Weber says.

After only three weeks in the HIRC program, Weber says he noticed an improvement in his ability to perform daily tasks.

"My organizational abilities have improved," he says. "The tasks here help me restructure my thinking from a helter-skelter thought process to taking notes and working from a main idea."

During one Monday's day-long treatment program, Weber moved from a group session, which focused on shifting attention, to a specialized therapy session in which he was asked to read a magazine article and retell the main ideas. Another group session was used to discuss brain functioning after head injury, while another stressed communication skills in interviewing others and retelling information.

Weber's individual life skills therapy session presented him with the task of making a grocery list, directing a driver to the grocery store and actually locating and purchasing the items. Other life skills ses-

sions have focused on following directions around the medical center, balancing a checkbook and other work-related tasks.

Weber will eventually be placed in a job therapy setting on the medical school campus. "The idea is to get him back in the workforce in an area where he'll be happy," explains Peggy Barco, an occupational therapist at HIRC.

Although Weber isn't sure what type of work he'll eventually do, he is glad to finally be getting some help for his previously invisible problem.

"We speak in the group about people not looking at brain injury as a real injury. When you see someone with a broken arm, you say, 'He's sick.' But when you walk out of the hospital with a brain injury, you're considered normal. You don't think about the impact it has on someone's life."

The HIRC program is designed to change patients' lives. "It's helping me recognize my deficit—my memory problem—and helping me deal with it more effectively," Weber says.

"I've been denying all these years that I have a problem. It's a heavy weight off my shoulders to speak about it. The feelings I'm able to express here have been locked up for 16 years. It's been really frustrating at times. People had thoughts about me as uncaring, unmotivated and floating around without direction."

Now Weber, as well as those around him, are looking at his life differently.

"I'm coming into a new perspective," he says. "I'm gaining insight into my strong points as well as my weaknesses."

The ultimate goal of the HIRC program is to return head injury patients to work or school. The program has graduated 14 patients, with 10 of them expressing a goal of returning to work. Three of these patients have not returned to work due to medical conditions. Of the remaining seven, six are working in some capacity.

For more information about the HIRC program, including patient admission requirements, call: (314) 652-8857. ■



Educating patients about the various functions of the brain and how this relates to their injury is one way in which the head injury staff helps patients adjust. As part of a lesson in

how the brain perceives sensory input, Bruce Crossen, M.D., asks Mark to close his eyes and guess what he's placing in his hand. Patient Marcella Gill looks on.



Detail of lung with emphysema.

Dr. Pierce flips through a three-ring binder of laminated lung tissue slices until he reaches a specimen that looks more like Swiss cheese than healthy human lung.

"This is the air sac wall of a smoker," he says, pointing to several large, gaping holes. "Notice how the connective tissues have been almost completely destroyed."

The emphysema patient from whom the tissue sample came probably didn't think about the connective tissues in his lungs until he started to lose them. Yet every breath he took depended on them, in particular on elastin—a cellular grouting between lung cells that gives the tissues their ability to contract and expand. As this precious material was scoured away by over-zealous white blood cells in their attempt to clean the aveolar walls of tar and other cigarette residues, the lungs lost their capacity for gas exchange.

The destruction of elastin in emphysema clearly illustrates how important the connective tissues are for normal tissue structure and function. "They hold you together, specify your shape, make sure that you maintain that shape, and that you change your shape the right way if it needs to be changed," says John J. Jeffrey Jr., Ph.D., professor of medicine and associate professor of biochemistry, who is one of more than a dozen School of Medicine researchers studying connective tissues.

The connective tissues—or extracellular matrix as they are referred to collectively—have become a hot research topic in the last five years, as more has been discovered about their role in tissue architecture, development, wound healing and disease. And because the body's many tissues are held together by a relatively small number of proteins, connective protein research has stimulated collaboration between investigators from a wide variety of disciplines, among them pulmonary medicine, dermatology, neurology and pathology.

Collagen

Jeffrey is using the uterus as a model to study the production and breakdown of collagen, a connective protein that lends strength to the skin, joints, tendons, lung and bone.

ISSUES

on

TISSUES

by Kathy Will

The uterus is an ideal candidate for the study of collagen regulation, according to Jeffrey, because of its enormous increase in size during pregnancy. He explains that the uterus is embedded in a collagen framework that protects the tissues of the uterus from rupturing as they expand to accommodate a developing fetus. This collagen framework enlarges with the expanding womb during pregnancy, requiring the production of tremendous amounts of collagen. Then, after delivery, this collagen is degraded, or involuted, more than eight times as fast as it took to accumulate it. "These processes are jealously guarded by biology," Jeffrey remarks. "It would be disastrous, for example, if the involutionary process were somehow turned on in the eighth month of pregnancy."

Jeffrey is interested in the mechanisms by which the collagen framework guards itself against the untimely onset of degradation, as well as the mechanisms that initiate degradation following delivery. These mechanisms involve the production and regulation of collagenase, an enzyme that is specific for breaking down collagen. As a biochemist working in a dermatology division, Jeffrey hopes to eventually apply what he learns about uterine collagenase regulation to the skin. Collagen makes up about 90 percent of the skin's structural proteins, and collagenase is known to be a key player in wound healing, according to Jeffrey. "But the skin is a tough nut to crack."

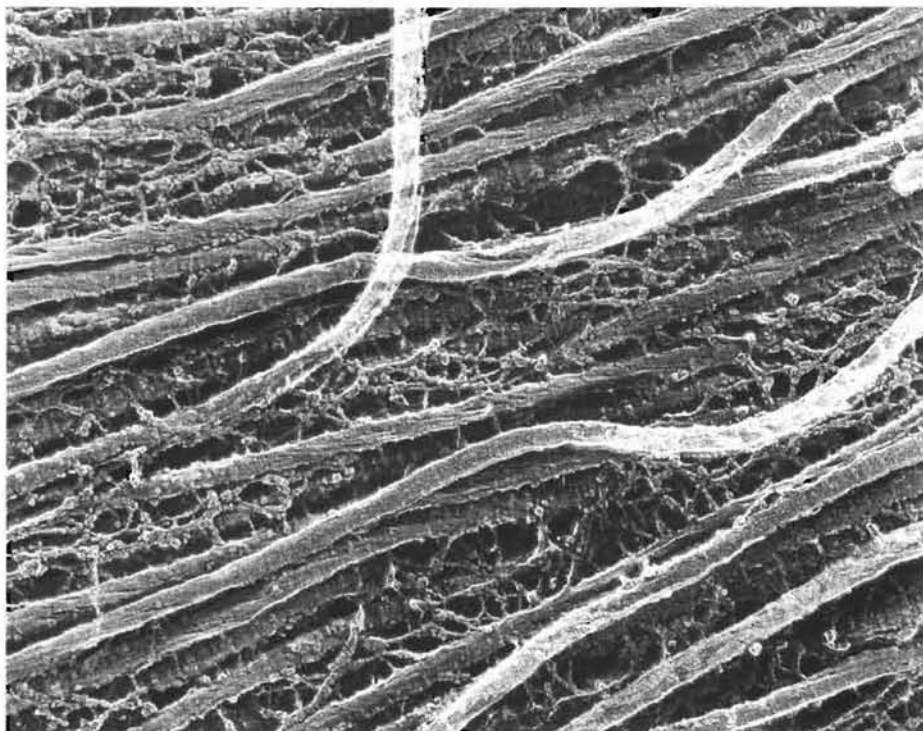
Howard G. Welgus, M.D., associate professor of medicine, would tend to agree. A dermatologist, Welgus also studies the degradation of collagen, but in fibroblasts of the skin and lung. There, he is tracing the action of collagenase and its inhibitor, tissue inhibitor of metalloproteinase (TIMP).

TIMP enables collagen synthesis and degradation to occur right next to one another, Welgus explains, by shielding selected areas of collagen from the action of collagenase. He believes that a better understanding of this process may shed some light on what's going wrong in diseases where not enough collagen is degraded, such as scleroderma and pulmonary fibrosis. It may help as well in diseases where too much collagen is degraded—emphysema and rheumatoid arthritis, for example.

Robert P. Mecham, Ph.D., associate professor of medicine and of cell biology and physiology, is also studying collagen

in the lung, but he is interested in production, in particular the over-production, of collagen in persistent pulmonary hypertension—a condition that affects one in approximately 1,500 newborns.

Mecham explains that, while the blood pressure in the lungs of developing fetuses is very high, it drops dramatically at birth. If a child is born with lungs that are not functioning properly, the oxygen levels in the lung are often low. The blood vessels in the lung ordinarily respond to low oxygen by contracting in those areas, Mecham explains, which forces the blood into areas where oxygen is more plentiful.



Freeze-etch of collagen fibers shows the helicoidal, or "twisted rope," organization of the individual collagen subunits. See note at end of story.

But if the entire lung of the newborn has low oxygen, the blood pressure in the lung remains high because the vessels never dilate and may even constrict. If the pressure remains high for two to three days, the vessels will begin to remodel themselves. During remodeling, the blood vessels lay down more collagen and elastin than they should, locking themselves into the constricted state so that the infant might not recover.

Using the blood vessels of cow lungs as a model, Mecham has successfully identified the cell type responsible for the remodeling—the smooth muscle cell. "Not only does it lay down collagen and elastin, but it instructs all the cells around it

to lay down collagen and elastin as well," he says. Mecham is currently trying to find out what causes the smooth muscle to remodel the vessel. "If we can understand what it is that changes the smooth muscle cell to begin with; if we can prevent that change, then perhaps we can prevent the subsequent remodeling in that vessel," he says.

Edmond C. Crouch, M.D., Ph.D., assistant professor of pathology, is also studying the regulation of collagen production. Crouch studies collagen production in pulmonary fibrosis, a disease in which there are abnormalities in the

amount and distribution of matrix proteins. He is particularly interested in the role of basement membrane damage. Defects in the basement membrane allow cells that are normally found within the alveolar wall to enter the airspaces of the lungs, where they become inactivated and deposit collagen and other connective tissues. Crouch would like to understand how these are signaled to make the proteins.

While Crouch's own work focuses on collagen production, he emphasizes the importance of looking at collagen degradation as well. "The tendency in connective tissue research is to work on one side of the fence or the other," he says. "We

definitely need to start trying to put it all together."

Degradation and production are both critical in bone remodelling, according to Steven L. Teitelbaum, M.D., Wilma and Roswell Messing Professor of Pathology, who explains that bone maintains and reshapes itself through a teeter-totter relationship of resorption and replacement, a delicate balance of breaking down and rebuilding.

In resorption, specialized bone-eating cells called osteoclasts, which are related to white blood cells called macrophages, attach themselves to the bone's surface. There they create an acidic environment that eats away the mineral and provides the correct milieu for enzymes to degrade collagen. The simultaneous digestion of mineral and collagen creates an indentation in the bone's surface. Areas of bone eaten away by osteoclasts are then re-filled with new collagen and mineral by cells called osteoblasts.

An imbalance between resorption and replacement gradually develops with age, according to Teitelbaum, resulting in osteoporosis, or the "brittle bones" of old age. Osteoporosis may also result at an earlier age if there is increased osteoclast activity, decreased formation of new bone or if an individual begins with less bone

mass. This last factor is particularly common in white women, the group most often affected by osteoporosis.

Teitelbaum is currently investigating two factors that accelerate resorption: parathyroid hormone and vitamin D. Parathyroid hormone speeds resorption by causing osteoblasts to activate the osteoclasts, while vitamin D may increase resorption by ordering macrophages to differentiate into bone-digesting osteoclasts.

Elastin

During the late 1940s, several prominent members of the School of Medicine faculty, including Morris Alex, M.D., assistant professor of clinical medicine, performed innovative studies on the connective protein elastin in the systemic and pulmonary arteries. Partly because of that work, John A. Pierce, M.D., Selma and Herman Seldin Professor of Pulmonary Medicine, became interested in the collagen and elastin in the lung. At that time, emphysema was recognized as a disease of those who smoked cigarettes.

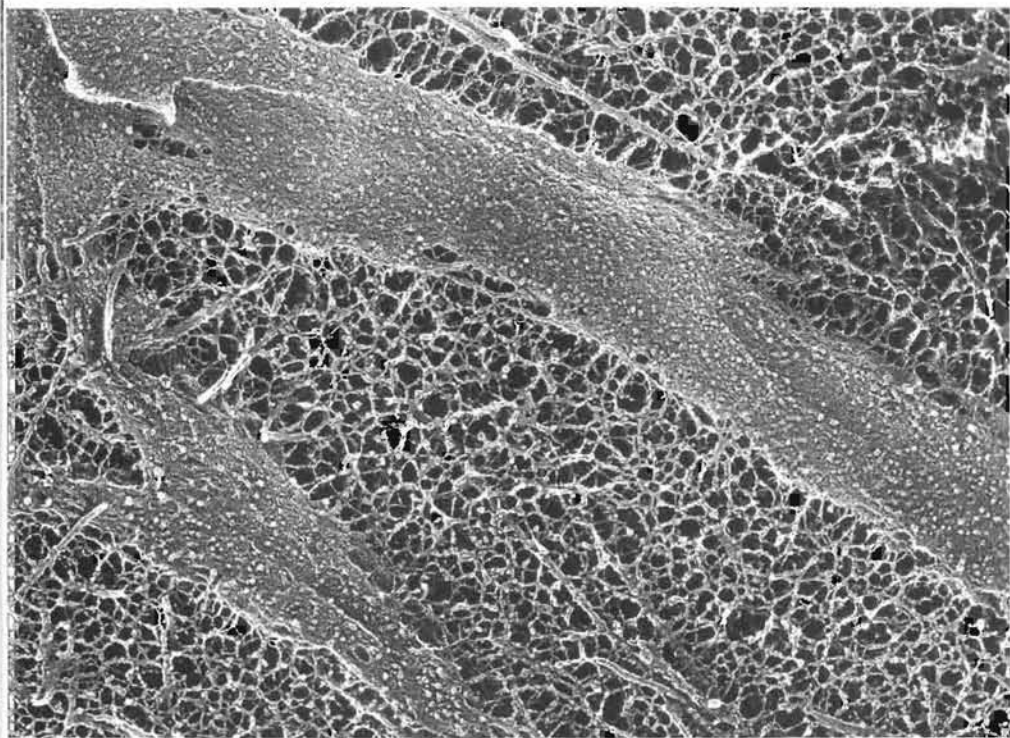
By 1963, it was discovered that a small number of people (about one in 5,000 in St. Louis) inherit a deficiency of alpha 1-antitrypsin—a protein that ordinarily protects elastin from breakdown by the enzyme elastase. And this deficiency pre-

disposes them to emphysema whether they smoke or not. Individuals who lack alpha 1-antitrypsin and smoke, typically develop emphysema during their late 20s or 30s, and often die of it before age 50, according to Pierce, who was one of the first individuals in the country to study alpha 1-antitrypsin. Antitrypsin deficient subjects who do not smoke, on the other hand, vary greatly in their tendency to develop the disease, and many never do.

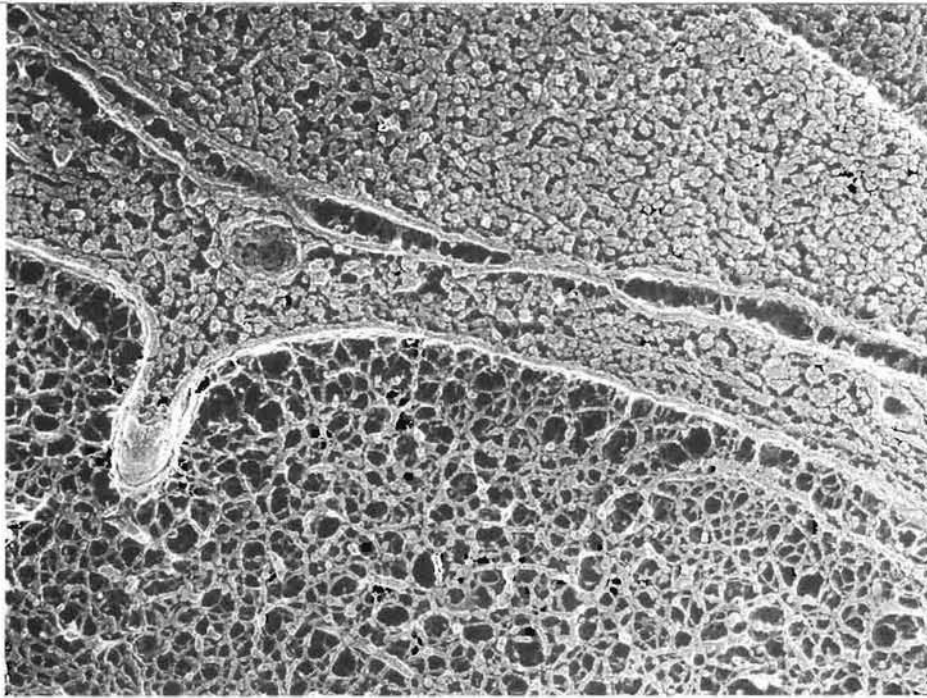
The association of alpha 1-antitrypsin with emphysema led scientists to wonder if smoking causes emphysema by somehow interfering with alpha 1-antitrypsin's ability to protect elastin in the lung. And since it was already well established that smoking produces a low-grade inflammation in the lungs, they suspected that the inflammatory response was involved. Upon further investigation, it was discovered that white blood cells called neutrophils contain large amounts of elastase, according to Robert M. Senior, M.D., professor of medicine, who was one of the first people in the country to demonstrate that emphysema can be induced in laboratory animals by injecting elastase from human neutrophils into their windpipes.

"Something important happens at those sites where white blood cells touch connective tissues," according to Edward J. Campbell, M.D., assistant professor of medicine, who is studying this interaction. "While the rest of the body remains protected by inhibitors, elastase and collagenase work together at sites where there are white blood cells." Campbell and others at the School of Medicine are especially interested in finding out why smoking causes lung disease in some, but not in others. He suspects this may have something to do with a variation in the number or the activities of white cells in the lung, and is studying this possibility.

Too much elastin can be just as harmful to tissues as too little, according to Mecham. Having studied the basic properties of elastin since he was an undergraduate, Mecham is currently investigating how too much elastin alters the mechanical properties of blood vessels and lungs. In atherosclerosis, injury to cells in the artery wall cause smooth muscle cells to behave as if they were healing a wound, he explains. But they overdo it by continuing to lay down elastin and collagen until they occlude the vessel. Mecham is trying to find the biochemical signal that directs the smooth muscle cells in this wound healing process. "If such a



High magnification of extracellular matrix between cartilage cells shows large, irregular elastin fibers with more narrow, straight collagen fibrils.



Freeze-etch view of ear cartilage shows a cell with surrounding extracellular matrix. The extracellular matrix consists of a finely woven meshwork that adjoins the cell membrane.

signal is found, we can then start thinking about intervention to reverse the process," he asserts.

Other Proteins

For years, scientists have studied connective proteins in their more static role as cellular cement. In the last five years, however, connective proteins have been identified as key players in tissue development, regeneration and repair.

John A. McDonald, M.D., Ph.D., associate professor of medicine and assistant professor of biological chemistry, and Alan L. Pearlman, M.D., professor of neurology and of cell biology and physiology, are studying the connective protein fibronectin, which directs the differentiation and movement of cells during development and wound healing.

McDonald is looking at the role of fibronectin in acute lung diseases such as pulmonary fibrosis and adult respiratory distress syndrome, which are characterized by excessive accumulations of connective tissue, or scarring. He believes that fibronectin may play an important role in these diseases as it does in wound healing, by aiding the deposition of collagen and attracting inflammatory and connective tissue-producing cells to sites of injury. "Increased production of fibronectin by lung cells at sites of injury is a common, if not universal finding in acute lung disease," he says. McDonald is currently investigating whether or not fibronectin attracts collagen-producing cells

into the airspaces of the lung, and ways in which fibronectin organizes itself into a fabric-like matrix.

Pearlman is looking at fibronectin's role in the organization of one of the most complex areas of the brain—the cerebral cortex. For a long time, neurobiologists believed that the brain never contains connective tissue. Pearlman's laboratory, however, was the first to show that fibronectin is present at specific times and in specific places in the cerebral cortex, and that its presence is correlated with the formation of the first connections between the brain stem and the cortex. In embryonic mice, fibronectin is found in the cerebral cortex shortly after the first week-and-a-half of development, and disappears about six days later, just before birth. This is approximately equivalent to the fifth through seventh weeks of human development. Pearlman believes that during its limited stay in the brain, fibronectin may serve as a highway, providing guidance for arriving nerve fibers as they grow towards the cerebral cortex.

The implications of his work are intriguing. "If we can learn how connective proteins help to form the initial connections between brain cells, we may be able to devise some scheme for enhancing brain regeneration following injury," he says. "As it is, the brain has a severely limited capacity for regeneration."

Peripheral nerve cells have a much larger capacity for regeneration than those in the brain, because they retain their con-

nective proteins after birth. Joshua R. Sanes, Ph.D., associate professor of anatomy and neurobiology, is studying regeneration at the neuromuscular junction between nerve and muscle. More specifically, he is looking at ways in which a variety of connective proteins help to guide nerves back to their muscles when they become detached.

Connective proteins are also essential for the formation of the myelin sheath that surrounds nerve cells and speeds conduction, according to Richard P. Bunge, M.D., Beaumont-May Institute of Neurology Scholar in Anatomy and Professor of Anatomy and Neurobiology, and Mary B. Bunge, Ph.D., professor of anatomy and neurobiology. Their work has emphasized the importance of connective tissue proteins within the trunks of peripheral nerves. A new concept emerging from this work is that the Schwann cell, previously thought to function primarily as the source of myelin around nerve fibers, is a major producer of connective proteins within peripheral nerves as well. Unexpectedly, they have found that these myelin-forming cells must form connective proteins before they can undertake their function of myelin production. No such constraints limit myelin formation in the central nervous system, pointing to differing roles of connective proteins in the central and peripheral nervous systems. Understanding these differences, they maintain, will be important in better comprehending differences in the capacity for regeneration in the central and peripheral nervous systems. ■

Using a unique way to view cells and their components in the electron microscope, John Heuser and Robert Mecham have been studying the organization of extracellular matrix and its relationship to cells. This technique, called quick-freeze, deep-etch, is particularly suited for this type of study since it avoids many of the artifacts inherent in standard methods of preparing samples for electron microscopy. Because the technique provides three-dimensional surface views of macromolecular structures that have not been subjected to chemical fixation or staining, the images obtained provide a truer representation of the physical relationships between matrix and cellular macromolecules than can be obtained using traditional methods for visualizing macromolecules in the electron microscope.

THE NIH *at 100 years*

BY PAUL G. ANDERSON

The first research grant awarded to Washington University School of Medicine by the National Institute of Health—there was only one in those days—was presented in 1938 to Dr. Edmund V. Cowdry, head of Cytology, for a study on the cytology of leprosy. Modest even for those times, the \$2,500 award marks the beginning of a relationship that has transformed medical science at Washington University, as it has at other universities, hospitals and laboratories throughout the United States.

Of all the School of Medicine faculty in the late 1930s, Cowdry enjoyed the widest contacts with private and public sources of research funding. All told, eleven of the thirty-three grants received by Washington University School of Medicine in the lean Depression decade (1929-1938) were won by Cowdry or faculty and staff from laboratories reporting to him.

In his application to the NIH for support in the leprosy study, Cowdry indicated that the purpose would be "to investigate the sequence of changes in organisms and cells as the lesions of human leprosy develop, with a view to providing a basis on which effects of treatment can be determined; to make parallel studies on the acid-fast bacterial disease of rats." The grant was renewed for a second year in 1939. During that period, Cowdry obtained permission to experiment with Promin, a preparation of glucosulfone sodium developed by the Parke Davis Company. His findings contributed to preparations for clinical trials of the drug at the Leprosy Hospital in Carville, Louisiana, where Promin was shown to be an effective therapy.

Before considering further details relating to Cowdry's work, it is worth noting that his leprosy grant was made at the

very midpoint of the hundred-year NIH history that was celebrated last year.

The NIH began in 1887 as a bacteriological laboratory at the Marine Hospital on Staten Island, New York. At that point, the Marine Hospital was already almost a century old, having been founded in 1798 by the federal government for the relief of sick and disabled seamen. The genesis, then, of what is now recognized as "one of the truly remarkable social inventions of the ages" was not only modest, but also incredibly slow.

The late 1930s witnessed dramatic changes in federal government policies toward medical research that followed in the wake, so to speak, of earlier New Deal programs. Up to then, the Franklin D. Roosevelt administration had not generally been receptive to social innovations beyond those designed to stimulate employment and economic recovery. So although the National Institute of Health re-



Top left: Evarts A. Graham, M.D., former head of surgery, recounts achievements in thoracic surgery for medical students.

Top right: Wendell Scott, M.D., former professor of radiology and President of the American Cancer Society, addresses an American Medical Association meeting in 1964.

Left: Edmund V. Cowdry, M.D., at his microscope.

ceived its name and authorization for a slightly expanded research program in 1930, it limped through the Depression years on total annual budgets of less than \$100,000.

Medical research made major strides with the passage of the National Cancer Institute Act in 1937, which appropriated nearly one and a half million dollars, including money for extramural research. This sudden largesse was a reaction, in part, to the exaggeration of the mysterious and sinister aspects of cancer by the popular press. Underscoring its special mandate, the NCI was established as a Public Health Service agency separate from the NIH (and would remain so until 1944).

Cowdry was among the first in St. Louis to apply for an NCI grant. He and his associates in the School of Medicine had been engaged in cancer research

for several years, notably in a series of investigations employing microincineration techniques. In 1937 he assumed, in addition to his other responsibilities, the position of research director at Barnard Free Skin and Cancer Hospital, and sought funding for the programs there. Barnard Hospital at that time was located in midtown St. Louis (Washington and Theresa Avenues) and was not formally associated with the Washington University hospital group, although many of the staff had medical school appointments. Cowdry, working with the advice and assistance of his predecessor at Barnard, Dr. Major G. Seelig, planned studies involving experimental carcinogenesis. In 1939, the NCI awarded his group \$5,000 to investigate "the cellular changes in the epidermis of mice painted with carcinogenic agents."

This proved to be only the first of several NCI or NIH grants Cowdry helped to secure for Barnard Hospital, where he remained as research director until 1948. This funding proved to be a significant factor in the decision to link Barnard with Washington University, overcoming protracted opposition to the idea from some members of the hospital board. In 1948, the president of the board, John R. Shepley, was informed by the NCI that consideration of further applications would be deferred, "in order to see if the conflict of opinion in St. Louis concerning affiliation with Washington University could be resolved." Shepley responded to the NCI with assurances on behalf of the board that "We are determined to see this matter through to a successful conclusion. . . . We believe that Barnard Hospital can render better care to patients and contribute



Above: The Barnard Free Skin and Cancer Hospital at its old location on Washington Avenue.

Far right: Arthur Kornberg, M.D., in his lab.

Right: William H. Danforth Sr. and Edmund V. Cowdry, M.D., discuss some of the first cancer studies.



more to research and education in affiliation with Washington University School of Medicine than as an isolated hospital." This objective was formally brought about that same year.

The NCI legislation was innovative for providing not only extramural research funds, but also training fellowships. Medical school deans and cancer experts throughout the country were asked for advice about its operation. Dr. Philip A. Shaffer was then dean of the School of Medicine. Both he and the renowned head of the Department of Surgery, Dr. Evarts A. Graham, were unanimous in their general support of federal funds for medical education, but also joined in expressing "misgivings" about what they perceived as restrictions to the program. In brief, they feared that recipients of the fellowships would become overspecialized, while students outside the program and physicians already in practice would be denied its benefits.

Once the programs actually began, most objections or misconceptions such as these were resolved. Reorganizations of federally funded medical programs under the aegis of the Public Health Service also helped to make clear their purpose and benefits to the extramural community.

In 1943, the NIH was given bureau status in the Public Health Service. The Public Health Service Act of 1944 consolidated existing programs under the NIH and gave the bureau general authority to conduct research.

In time, virtually everyone with a serious research agenda began applying for NIH grants. Included were scientists who had enjoyed long and fruitful careers without the aid of major outside funding. Dr. Joseph Erlanger, for example, who had been at Washington University since 1910 and was a recipient of the Nobel Prize in 1944, applied for his first NIH grant upon his retirement two years later. The title of Erlanger's project reads with disarming candor "Nerve physiology along lines 'director' was pursuing prior to his retirement as head of the Department of Physiology July 1, 1946." The Physiology Study Section approved a sum of \$1,000, which was paid in 1947, with subsequent renewals awarded to him through 1951.

In 1946, the Division of Research Grants was established to handle the flood of applications pouring in from institutions across the country. The Division was instructed by its advisory body, the National Advisory Health Council, to estab-

lish "study sections" in appropriate specialties to evaluate the merit of the applications. This mechanism, later developed to include different levels of peer review for both grant and contract projects, operates to this day, with most study sections, or scientific review groups, covering specific scientific disciplines or disease areas.

A second level of review is performed by a national advisory council or board for each institute or division of the NIH. Over the years, scores of Washington University School of Medicine faculty have joined with colleagues from other institutions to serve as members of NIH advisory groups. Most observers concede that the system has operated overall with the highest possible standards, both in terms of scientific judgment and of impartiality.

It is important to remember in this context that the NIH has never discontinued its own intramural research programs. Located chiefly in Bethesda, Maryland, the NIH laboratories and related facilities today constitute one of the largest medical research complexes in the world. Interactions between NIH scientists and their colleagues outside the organization have always been highly significant.

The distinguished career of Dr. Arthur Kornberg provides an excellent example in this regard. Kornberg joined the NIH during World War II. After the war, he was granted leave for fellowships, first at New York University with Dr. Severo Ochoa in 1946, then a year later with Drs. Carl Cori and Gerty Cori in the Department of Biological Chemistry at Washington University. Kornberg credits these noted scientists for providing him with crucial direction and encouragement in his early research on enzymes. In 1953 he left the NIH to join Washington University as head of the Department of Microbiology, a position which he held until 1959. In that year, he and Ochoa were awarded the Nobel Prize for the enzymatic synthesis of RNA and DNA.

Another Washington University scientist who enjoyed particularly long and varied connections to the NIH has been Dr. Robert E. Shank, professor emeritus of internal medicine and former head of the Department of Preventive Medicine and Public Health. Shank served as a special consultant in nutrition to the Public Health Service (1949-1953); member of study sections in public health research (1953-1956), human ecology

(1959-1964), and nutrition (1964-1968); member of advisory committees or councils on epidemiology and biometry (1956-1959), gastroenterology and nutrition training (1968-1969), child health and human development (1969-1973), and clinical applications and prevention (1976-1980); and chairman of the Review Committee for Clinical Nutrition Research Units (1979-1981) and the Policy Advisory Board of the National Heart, Lung, and Blood Institute. Shank's career also illustrates certain international ramifications of the NIH. Through his work in Bethesda, Shank was asked to serve as a nutritionist on U.S. government projects overseas, notably in Peru and in Brazil.

Having discussed the involvement of some of Washington University School of Medicine's most prominent faculty in NIH programs, it is also important to recognize that federal grants and contracts are extended to investigators who are relative beginners in medical research. Typical, indeed, is an investigator who, as an assistant professor, is a first time recipient of a five-year grant. None of the School of Medicine's preclinical or clinical departments could have operated as it has for the past four decades without the salaries of many scientists and technicians paid in part by the NIH. Even in instances where research funding has largely been derived from private sources, NIH assistance in various forms is a significant factor. Such assistance ranges from the use of equipment paid for by earlier federal grants to information gathered from any of the more than twenty databases originating with the National Library of Medicine, a branch of the NIH.

Still, general competition for NIH dollars and inflation of grant and contract funding pose a constant and serious challenge. Even more problematic are the constraints placed on federal spending that have grown increasingly pronounced in the 1980s. The small, yearly battles over who gets the grants and who doesn't, however, can in no way diminish the ground that has been gained by the NIH in its war on disease.

Washington University School of Medicine looks back on the 100th anniversary of the NIH with celebration, while looking forward to the next 100 years with anticipation.

PHYSICIANS ABROAD

B Y C A N D A C E O ' C O N N O R



IMAGINE

walking into a hospital room to check a patient's progress, only to find his entire family crouched on the floor, cooking over a charcoal fire. Or fancy treating an 11-year-old girl who is about to return to her village—for her upcoming wedding.

Physicians who volunteer in Third World countries encounter surprising cultural differences. They also face difficult medical problems: leprosy, parasitic diseases, rare eye conditions, sleeping sickness. In an operating room, equipped only with surgical essentials, they may struggle to correct an adult's cleft palate or a child's severe burn deformity.

*Operating by flashlight. Photo by
Lawrence Gans, M.D.*

The need is vast, at times overwhelming. "You have to learn that you can't change conditions. You have to accept the reality and do what you can," says Samuel Logan, M.D., assistant professor of plastic and reconstructive surgery at Washington University School of Medicine.

Logan is one of the school's faculty and staff members who, in recent years, have taken time away from their training or careers to volunteer abroad in a medically deprived country. They have traveled to different destinations on a variety of programs, and have been prompted by such diverse motives as altruism, a spirit of adventure, religious conviction or love of travel.

Yet without exception, they all recommend the experience. In one way or another, it has changed their lives. "It was extremely rewarding," says Neville Grant, M.D., professor of clinical medicine, who spent four months in Africa at Albert Schweitzer's hospital. "Not only before and during, but many times since then."

In this article, four School of Medicine physicians describe their overseas experiences. None has sought publicity; in fact, they all hesitate to take credit for their work, since so much remains to be done.

"You feel as though you should still be there," says Charles Miller, M.D., a dermatologist and instructor in clinical medicine. "When you see how much there is to do, what you did seems insignificant. It just wasn't enough."

LAWRENCE GANS

In the Third World, blindness is not just a personal tragedy. It can also have a major impact on a country's economy. Of 100 million people in Bangladesh, for example, one million are blind, some two-thirds from cataracts. All these potentially productive people are snatched from the labor force.


"But if you remove the cataracts and put a lens implant in a patient," says Lawrence Gans, M.D., assistant professor of ophthalmology, "you've taken a person who's totally dependent on family and friends and made him an independent and functioning human being."

In the past two years, Gans has made eight trips to distant parts of the world to treat eye patients and train local physicians in the latest surgical techniques. The teaching is critical. "If I can show 10


doctors in Bangladesh how to do intraocular lens implant surgery, there are thousands of patients I've ended up helping," he says.

Gans travels under the auspices of Project ORBIS, a nonprofit group that has outfitted a DC-8 airplane as a state-of-the-art eye hospital. On board are an operating room and laser treatment area, along with classroom space and an audio-visual studio containing all the latest technology.

By using a jet, ORBIS has neatly disposed of many difficulties inherent in international medicine. The plane generates



"I have a picture of the chief surgeon operating in his T-shirt inside a schoolhouse. The windows were open and birds were flying overhead; extra light came from uniformed Boy Scouts holding flashlights."



its own power, so there's no problem with fluctuating power levels or different voltage requirements. And it carries a large supply of water and a sophisticated purification system.

Gans made his first trip in 1985, when ORBIS asked him to help set up an eye-bank in Bangladesh for corneal transplant surgery. Since then, he has demonstrated microsurgical techniques in the Philippines, performed corneal transplant surgery in Morocco and treated advanced glaucoma in Jamaica.

"The level of information we exchange depends on the country," Gans says. "In Singapore, a very modern and advanced place, they're not interested in learning the basics of cataract surgery. The exchange there is similar to Grand Rounds at Washington University or an American academy meeting."

Wherever he goes, doctors bring in extraordinary cases sure to interest him. He sees hereditary conditions so rare that only a handful exist in the world, infec-

tions usually found only in textbooks, eye diseases that have progressed to a stage undreamt of in the U.S.

Help sometimes comes too late. His slides show a Colombian teenager with white, opaque, unseeing eyes. She has Stevens-Johnson Syndrome, which causes severe dryness and scarring on the surface of the eye. At an earlier stage, the disease could have been arrested. "Now her eyes have essentially turned into leather," Gans says.

Yet there are also victories. A 12-year-old Jamaican boy, who had lost his vision at age six, was languishing in a school for the blind. An indigent child on an island with only a handful of eye doctors, he had little hope. Then ORBIS discovered him, diagnosed his congenital corneal dystrophy and provided a corneal transplant to help restore his sight.

"Within three weeks after surgery, he was helping the other kids at the school to eat and get around," Gans says. "Within two months, he had gone home to take care of his family, who were also blind."

While most surgery takes place on the ORBIS jet, Gans occasionally travels to local hospitals, where he helps doctors adapt complex procedures to equipment they have on hand. In a pinch, he says, an intravenous catheter will do for cataract surgery. A friend taught Thai doctors to use a fish aquarium pump to remove cloudy fluid from the eye.

Gans has developed great respect for the dedication and ingenuity of most local physicians. In Bangladesh, a team of ophthalmologists travels to rural communities where they remove hundreds of cataracts each day, often under primitive conditions.

"I have a picture of the chief surgeon operating in his T-shirt inside a schoolhouse. The windows were open and birds were flying overhead; extra light came from uniformed Boy Scouts holding flashlights," Gans says. "They did 20 cases in an hour, three tables at once, with unsterilized instruments that were only washed and rinsed in boiling water between patients. Yet in 20 cases, they had just one minor complication."

Next year, Gans will make two trips to Asia and Africa. His wife, a nurse, often accompanies him. It's a kind of working vacation, he explains, which fulfills their love of travel. Do they come back exhausted? "No," says Gans, "Actually, it's rejuvenating. It's a very euphoric kind of thing to do."

SAMUEL LOGAN

Samuel Logan has good reason to remember all three trips he has made to church-run jungle hospitals in Bangladesh and Indonesia. On the first, as a medical student, he met his future wife. On the second, as a resident, he changed his choice of career. And on the third, this past year, he handled some of the most challenging surgical cases he has ever seen.

But threaded through all his memories are the faces of patients who came hundreds of miles by rickshaw, by boat, by bus or on foot to seek treatment that is often years overdue. Children are the most poignant. "The kids have a special place in your heart," he says, "because they are so helpless."

In Indonesia, Logan saw a 10-year-old girl with a cleft lip and palate, unrepaired from birth. In Bangladesh, he saw an 8-year-old, whose hand was frozen and contorted by severe burns, an injury she had probably lived with since infancy when, like many native children, she had fallen into a cooking fire.

On Logan's second trip to Bangladesh, he helped a 7-year-old named Saleem, who was in desperate need of a skin graft to cover his badly burned neck and chest.

Nine years later, Logan saw Saleem again. The boy had healed well, but required touch-up surgery. Logan prizes a photo of himself with his happy patient. "If I go back, I hope to look him up and see how he's doing," he adds.

Logan was a medical student at UCLA in 1973, when a lecture at his church introduced him to the idea of overseas service. The speaker was Viggo Olsen, M.D., a brilliant surgeon who had given up a stateside career to open a 50-bed Baptist mission hospital in a poor, remote and politically troubled part of East Pakistan (now Bangladesh).

Deeply touched by that description of hardship and need, Logan decided to spend part of his fourth year at Olsen's Memorial Christian Hospital. But another student had already volunteered for the same slot. Logan agreed to come for a week-long visit, then spend three months at Bethesda Hospital on the island of Borneo (now Kalimantan-Barat) in Indonesia.

That first week changed his life. Across the room one day he spotted a surgical nurse from Ohio, who had come to the hospital two years earlier to do mission



Hospital ward in Bangladesh. Photo by Samuel Logan, M.D.

work. "It was a whirlwind courtship," Logan says. "We corresponded after I went on to Indonesia; we met in Singapore; we came home for my graduation and were married three months later."

A research period during Logan's surgical residency gave the couple a chance to return to Bangladesh in 1978. Their six-month stay turned into a year as Logan treated more than 400 cases, many more difficult than anything he'd seen in the U.S. Among the first was cleft lip surgery on a 41-year-old man.

During that trip, Logan gave up his ambition to specialize in cardiac surgery. Olsen had warned him that such expertise was of little help in underdeveloped nations: They would rather fix 100 hernias than one heart, do more good for more people.

"I was a little disappointed until I realized that, with the background I had already, I could specialize in plastic surgery and become fully trained in general surgery as well. That would allow me to have a meaningful academic practice in the U.S. and help overseas in the future," Logan says.

He did just that this past winter when he and his wife, with their four small sons, paid a 12,000-mile visit to two overseas hospitals. A specialist now, he could treat the most complex cases and train staff doctors in the latest techniques. His help was sorely needed.

Within minutes of leaving the light plane which brought them to Indonesia,

Logan was in the operating room. In one week he did 12 major operations, including the removal of a huge, 2-pound 12-ounce parotid tumor from the side of one man's face. To cover the area, Logan performed what may have been the country's first myocutaneous flap.

Even this serious work had its lighter moments. One patient had a total of 26 digits: six fingers on each hand and seven toes on each foot. "He said he liked having six—that meant good luck—it was the *seventh* he didn't like," Logan recalls. "So we took off his second great toe and made a cleft between the first one and the next toe, so he could wear sandals," Logan says.

Back home now, Logan still helps in whatever way he can. He persuaded Zimmer Corporation to give the Indonesian hospital a much-needed surgical "mesher" to stretch skin grafts used on burn patients. Operating room nurses at Barnes collect old sponges which he sends abroad for sterilization and use, and he and his wife speak at churches about their experiences.

Someday—perhaps on vacation or on sabbatical, Logan will go back. "The experience gets in your blood," he says. "I love Barnes. I love St. Louis. I like my house and my cars. But somehow, deep inside you, once you see the need and have an opportunity to contribute to people's well-being, it's something you never get over."

NEVILLE GRANT

For most people, Albert Schweitzer is a symbol of saintliness: a gentle humanitarian who gave up brilliant careers in theology and music to devote his life to medicine at a small African hospital. But his full portrait is actually more complex. "People are shocked to hear Schweitzer called controversial. They don't understand it," says Neville Grant.

In 1954, while a senior at Columbia University School of Medicine, Grant became intensely curious about Schweitzer and his work. When he wrote asking whether he could come and help, Schweitzer replied that they'd be glad to have him. That's how Grant became the first medical student ever to assist at Lambaréné, where he learned to appreciate Schweitzer's rich and sometimes contradictory character. Far from the mild man of legend, Schweitzer was austere, distant and rather authoritarian. "While we were working, his philosophy was: 'Well, we have a job to do. There's no point sitting around talking about it.' So there was not a lot of interaction," Grant says.

Yet at mealtime he was often animated, speaking in his native Alsatian, a dialect of German. And late into the night, Grant could hear him in the adjoining hut, play-

ing the Bach that he loved so well on a piano fitted with non-functional foot-pedals, so that he wouldn't forget his organ footwork.

Schweitzer's hospital reflected his philosophy of life: plain buildings made of wood; simple and close to nature. "He didn't have a lot of modern equipment, partly because it wasn't there, and partly because he wasn't interested in getting it. He preferred not to introduce too much technology between man and nature," Grant says.

But he did have up-to-date medications to treat the tropic's devastating diseases: malaria, parasitic illness, sleeping sickness, leprosy. There was also elephantiasis, in which plugged lymph glands make legs swell so enormously that they resemble elephant legs. And children came in with bellies distended by kwashiorkor, a protein deficiency.

People visiting Lambaréné were sometimes disappointed to find Schweitzer the man, not Schweitzer the legend. Grant learned to appreciate his extraordinary qualities, as well as his humanity. "There were a lot of things he wanted to do and write," Grant explains, "and there wasn't much time left."

Grant was one of four doctors and five nurses on the staff at the hospital in

French Equatorial Africa (now Gabon). His job was to care for lepers in the new village, financed with the proceeds from Schweitzer's latest award, the 1954 Nobel Prize. It was a heady experience for a medical student, in spite of occasional crises.

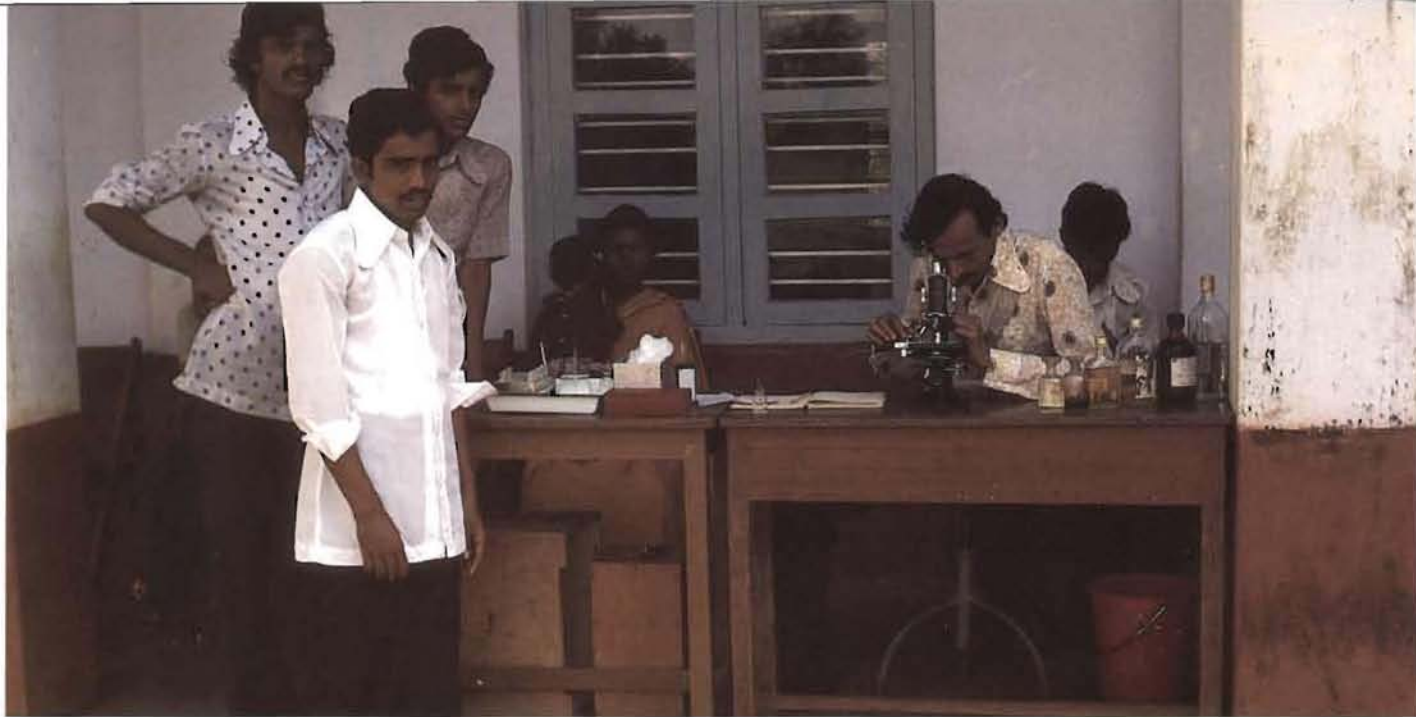
One such crises involved a female leper, who was having difficulty in labor. Trying to get her to the hospital, Grant gave her an injection to stimulate her uterus and bundled her into a canoe for the short trip up the Ogowe River. Half-way there, the baby arrived—and Grant managed to deliver the healthy infant without capsizing.

After leaving Africa, Grant interned at Washington University School of Medicine. Though Schweitzer invited him, he has never had an opportunity to return to the hospital. On his office wall, he has a photo of Schweitzer, who died in 1965, taken by the famous LIFE magazine photographer, Eugene Smith, who visited Lambaréné while Grant was there.

"There is controversy about Schweitzer, but to my way of thinking, it was nice to know that he wasn't a saint," Grant says carefully. "He was a strong personality with controversial aspects to him. In the final analysis, he was and remains an enormously significant person from whom we can all learn about life."



Drs. Neville Grant and Albert Schweitzer in 1954. Snapshot courtesy of Dr. Neville Grant.



Lab on a porch step. Photo by Charles Miller, M.D.

CHARLES MILLER

In 1978, Charles Miller went to India the hard way. After flying to London, he spent three months hitchhiking and hopping buses, trains or boats on a zig-zag path through Asia. His long journey helped reduce the devastating culture shock.

"As I moved across Asia, conditions became more desperate. But I was introduced to it gradually. By the time I got to India, I'd had several months of seeing obviously ill people and their poverty," says the 1972 School of Medicine graduate.

At the Kasturba Medical Center in the small town of Udupi on India's southwest coast, Miller spent three months as the only staff dermatologist. He trained physicians at the affiliated medical school and saw patients from the surrounding rural area.

Skin infections flourished in the tropical heat. Scabies, caused by mites burrowing under the skin, was also common. Other conditions, especially tuberculosis of the skin, were new to Miller. One five-year-old boy had already developed on his neck a TB-caused abscess the size of a baseball.

Before leaving for India, Miller attended a three-day seminar at the U.S. Public Health Service Leprosy Hospital in Louisiana to prepare for the many lepers he would find abroad. He also spent three weeks studying tropical dermatology at the All-India Institute for Medical Sciences in Dehli. At Kasturba, one day

each week was completely devoted to the care of lepers. Some patients bore few signs of the disease; others were missing fingers or noses.

"The disease can be arrested with drugs; if caught very early, it can probably be cured. To completely eradicate the disease organisms, patients must take medicine for a number of years," he says. "The problem was that people would take it for four or five months, then the disease would appear to clear up so they would stop. Six months later, it would come back—this time in a form resistant to the drug they had been taking."

Also complicating treatment was the lack of drugs and basic equipment and materials for culturing organisms, performing skin biopsies, even for doing some blood tests. Miller found it frustrating to see a problem and know he needed a biopsy for accurate diagnosis. But biopsies had to be saved for a handful of cases in which they made the biggest difference.

Another obstacle was the modesty of rural women. Once a week, the medical school sent its truck to a small town in the hills nearby and held clinic in the local schoolhouse. Under the gaze of curious children, Miller would screen patients outdoors, then send inside those he wished to examine.

"But a lot of women didn't want to be examined," he says. "They weren't used to having a doctor look at parts of their body. In one place, there was a nurse whose job it was to describe what the patient's skin looked like. That way the

women would not have to take off their clothes."

Political tensions in the region changed his plans to visit a CARE-run hospital in Afghanistan. "After finishing in India, I wrote to them and was told that the CARE program had been disbanded because of dangers associated with the increased Soviet presence. They were greatly concerned about what was going to happen to Afghanistan. So I decided not to go and, sure enough, shortly thereafter the Russians did invade," he says.

Back in St. Louis, Miller quickly resumed his practice. An ardent traveler, he also continued to take briefer trips to exotic places; all told, he has been to more than 100 countries. He and his wife, a speech pathologist who received a master's degree in communication disorders from Washington University in 1972, plan to volunteer abroad as soon as their two children are old enough.

Though he has seen many parts of the world, his Indian experience made a lasting impression. "I've never gotten over what I saw there," he says. "At least once a week, when I take a hot shower, I realize how many people can't do that. They need so many things that we simply take for granted." ■

Physicians and students interested in volunteering abroad can get more information through the Registrar's Office (362-6848) or the Barnes House Staff Office (362-1935).

STUDENT STAGE

Olin Foundation Creates Fellowships

The Division of Biology and Biomedical Sciences at the School of Medicine recently selected a dozen of their "best and brightest" to become the first of many Spencer T. and Ann W. Olin Medical Fellows.

Made possible by a \$30 million gift from the Spencer T. and Ann W. Olin Foundation, the new fellowships will provide support for aspiring medical researchers in the Medical Scientist Training (MSTP) Program, a six-year program that allows young people of exceptional quality and promise to simultaneously pursue the M.D. and

Ph.D. degrees.

Washington University's Medical Scientist Training Program, which was designed to help fill the continuing shortage of physicians who pursue careers in biomedical research, is generally regarded as the best of its type in the country. Last year, the program received approximately 300 applications for only 16 openings.

In addition to MSTP students, the new fellowships will also provide support for Ph.D. students in the medical sciences. The twelve new Spencer T. and Ann W. Olin Medical Fellows for 1987 are:

MSTP

Richard J. Auchus received the S.B. degree in chemistry at the Massachusetts Institute of Technology, where he earned a perfect grade point average in science. At Washington University, Auchus completed his pharmacology thesis on "14, 15-Secoestratrienes as Inactivators of Estradio Dehydrogenase from Human Term Placenta: Chemistry, Enzymology, Spectroscopy and Pharmacology" in the laboratory of Douglas F. Covey, Ph.D., associate professor of

pharmacology. He graduates this spring.

Mark Behlke received the B.S. degree in biology from the Massachusetts Institute of Technology, where he was a National Merit Scholar. During his first year at the School of Medicine, Behlke received the Carl T. and Gerty F. Cori Prize in Biochemistry. His thesis project, conducted in the laboratory of Dennis Loh, M.D., assistant professor of medicine and of microbiology and immunology, emphasized the molecular genetics of T cell receptor. He graduates this spring.



Olin daughter Mary Dell Pritzlaff is seated with 1987 Olin Fellows (front from left): Qiao Yan, Richard Auchus, Tommy Chu, David Sweetser and (back from left): David Burke, Roger

Inhorn, Jonathan Mink, Mark Behlke, Robert Heukeroth, Dwight Towler, Phyllis Faust and Megumi Taniuchi.

Tommy W. Chu graduated magna cum laude with highest distinction in biochemistry and received the B.S. degree from the University of Illinois. At Washington University, he completed his molecular biology thesis work in the laboratory of Arnold W. Strauss, M.D., professor of pediatrics and biological chemistry. Chu's project included the functional analysis of a mammalian mitochondrial import signal. He graduates next year.

Phyllis L. Faust received the B.A. degree in chemistry from the State University of New York at Potsdam, and completed her undergraduate work at Clarkson College, where she graduated summa cum laude in chemical engineering. Faust's integrative and cell biology thesis project includes the determination of a protein domain responsible for specific phosphorylation of lysosomal enzymes in the laboratory of Stuart A. Kornfeld, professor of medicine and biological chemistry. She received the Carl T. and Gerty F. Cori Prize in Biochemistry, during her first year of medical school. She graduates next spring.

Robert O. Heuckeroth received the B.S. degree in chemistry from the University of Maryland, where he graduated summa cum laude with high honors in chemistry. During the first year of medical school, he received the George F. Gill and Kehar S. Chouke Prizes in Anatomy. In his molecular biology thesis project, he is using fatty acid analogs to investigate the role of covalently bound lipid in protein targeting and function in the laboratory of Jeffrey I.

Gordon, M.D., professor of medicine and biochemistry. He graduates in 1990.

Roger C. Inhorn graduated with distinction and a perfect grade point average from the University of Wisconsin, where he received the B.S. degrees in molecular biology, mathematics and zoology. During his first year at the School of Medicine, he received the Carl T. and Gerty F. Cori Prize in Biochemistry. Inhorn is studying the enzymology of inositol phosphate metabolism in the laboratory of Philip W. Majerus, M.D., professor of medicine and biological chemistry. He graduates in 1990.

Jonathan W. Mink graduated cum laude with high honors in psychology from Wesleyan University, where he received the B.A. degrees in biology and psychology. While completing his neural sciences research project in the laboratory of W. Thomas Thach, M.D., professor of neurology and anatomy and neurobiology at Washington University, Mink was awarded the James L. O'Leary Prize for Research in Neuroscience. His thesis gives evidence that the output of the basal ganglia—those parts of the brain affected by Parkinson's Disease—serves to inhibit postural holding mechanisms in the brain stem. In Parkinson's Disease these postural holding mechanisms cannot be turned off, which may be a principal reason for the difficulty in making voluntary movements. He graduates next spring.

David A. Sweetser graduated with distinction from Stanford University, where he

received B.S. and M.S. degrees in biology. His molecular biology thesis project in the laboratory of Jeffrey I. Gordon, M.D., professor of medicine and biological chemistry, includes the use of transgenic mice to study gradients of gene expression in the mammalian intestine. He graduates next spring.

Megumi Taniuchi graduated summa cum laude from Yale University, where he received B.S. and M.S. degrees in molecular biophysics and biochemistry. While completing his neural sciences research project in the laboratory of Eugene M. Johnson Jr., Ph.D., professor of pharmacology at Washington University, Taniuchi was awarded the James L. O'Leary Prize for Research in Neuroscience. Taniuchi has also received the first place Mead Johnson Excellence of Research Award, the Roche Laboratories Award, the James E. Beall, II Award in Neuroscience and the AMA Award in Basic Science. His thesis project involved the use of a monoclonal antibody to study the structure of and regulation of the expression of the nerve growth factor receptor. He graduates this spring.

Dwight A. Towler graduated summa cum laude from Moorhead State University, where he received the B.A. degree in chemistry. During his first year of medical school, he received the Dr. Richard S. Brookings Medical School Prize, and his molecular biology thesis project included isolating and characterizing the enzyme responsible for adding a fatty acid myristate to certain

biologically important proteins. This work was completed in the laboratories of Jeffrey I. Gordon, M.D., professor of medicine and biochemistry, and Luis Glaser, Ph.D. adjunct professor of biological chemistry. He graduates next spring.

Doctoral Students

David T. Burke, a predoctoral student in the molecular biology program, completed his undergraduate work at the University of Rochester in Rochester, New York, where he received the B.S. degree in biology and biochemistry. Burke's research work includes characterization of the tyrosine transfer RNA gene family in the yeast *Saccharomyces cerevisiae*. More recently, Burke has developed a novel system for cloning and propagating large molecules of human genomic DNA with *Saccharomyces* as host organism. His dissertation advisor is Maynard Olson, Ph.D., professor of genetics.

Qiao Yan, a predoctoral candidate in the neural sciences program at Washington University, graduated from the Fudan University in the People's Republic of China with a B.S. degree in physiology. He then studied neuroscience and English at the Shanghai Brain Research Institute, and was awarded a scholarship for graduate study in the United States. Yan is conducting his dissertation research in the laboratory of Eugene M. Johnson Jr., Ph.D., professor of pharmacology. This work involves studying the role of neural growth factor receptors in rat neural development. ■

One Small Step Away

It's been years since Barry J. Linder, M.D. '84, played rocketship on the swings. Yet his fascination with outer space has remained constant from the swing set to his recent seat on the life sciences advisory committee for NASA's first manned space station.

"I just always liked everything to do with space, though I never seriously considered that my career would involve anything to do with space," says Linder, who has seen all three "Star Wars" and all four "Star Trek" movies on opening day, and watched all of the first six shuttle launches live. "It was just sort of a thing you see on TV."

Linder began to take his interest in space more seriously when he was selected as an intern at the Johnson Space Center in Houston, Texas for the summer following his first year of medical school. There he studied under William Thornton, M.D., a physician and astronaut who Linder still collaborates with and considers to be his most influential mentor.

That summer Thornton was investigating the pooling of blood that occurs in the legs of astronauts as they return to gravity. Linder explains that an astronaut's blood re-distributes towards his head as he leaves the earth's gravity, and towards his feet as he returns. But if the blood re-distributes into the legs too quickly, the astronaut may lose consciousness.

Temporary blackouts upon return to earth were not much cause for alarm before the advent of the shuttle, Linder explains, because all the astronauts had to do was lie in their capsules and be parachuted down. It became much more of a concern with the shuttle, which the pilot and co-pilot are required to land. "And they get only one chance to land," he adds.

Computer modeling studies of this problem, in which Linder was involved, helped NASA decide to clothe shuttle pilots in special anti-gravity suits that exert positive pressure and force blood out of the legs.

Since then, Linder has continued to collaborate with Thornton, who published an article in *Aviation Space Environmen-*

tal Medicine last September, in which Linder served as second author—"making me think that I was just one step away from being an astronaut," he says.

Their paper, which correlated the absence of bowel sounds with motion sickness, established Thornton and Linder as the first to record bowel sounds in flight.

Linder also designed the first space shuttle study of how weightlessness and space motion sickness affect pupil size, which Thornton used in his shuttle experiments. Linder's background in

"The vantage point of earth orbit would lead to global awareness which would protect us from war, other forms of environmental destruction and potentially self-annihilation."

engineering was a significant advantage in designing these studies.

Linder earned his bachelor's degree in engineering at the Massachusetts Institute of Technology, where he learned to apply engineering principles to physiology through a jointly-sponsored Harvard-M.I.T. program in bioelectrical engineering.

He later had the opportunity to experience the effects of zero gravity on his own physiology, while serving as a test subject on NASA's zero gravity plane, or "vomit comet," a military version of the 707 that drops from 30,000 feet to 10,000 feet in 30 seconds. "I brought back my vomit bags unused, I was happy to say," Linder recalls.

Upon receiving his master's degree in engineering from the University of Connecticut, Linder worked for one year as the biomedical engineer responsible for managing the installation and expansion of computer systems at Peter Bent Brig-

ham Hospital's Clinical Neurophysiology Laboratory in Boston. Then he applied and was accepted to the School of Medicine, where he became the first Albert J. Blanke Jr. Endowed Scholarship Fund recipient and received the Dean's letter of commendation for high scholastic standing.

After medical school, Linder completed his internship in internal medicine at St. Luke's Hospital in St. Louis, and served one year as a National Eye Institute Post-doctoral Trainee in the Visual Sciences Training Program. As a trainee, he explored the usefulness of visual electrophysiological tests in diagnosing and detecting disease, as well as the effects of a loss of gravity on these tests. One year later, he entered the ophthalmology residency program at Barnes Hospital, which he will complete in 1989.

Last January, Linder was selected by NASA to be a staff assistant for the Operational Medicine Study Group in the NASA Life Sciences Strategic Planning Study Committee of the NASA Advisory Council. With 17 members covering 11 study groups, the committee was formed to address what needs to be done in the life sciences to support advanced space missions. Such missions will likely include lunar base missions, manned missions to Mars and travel to and work on a permanently orbiting research and work center.

Scheduled for completion sometime in the next decade, the permanently manned space station, together with a fleet of space shuttles, will enable six to eight individuals to travel and stay in space for extended periods of time. But before NASA can send people on such long-term missions, it needs to define and address the health risks associated with long stays in space and outline the medical and health needs of the astronauts. These are issues of operational, or space medicine.

As a staff assistant for NASA's Operational Medicine Study Group, Linder has attended full committee meetings in Houston, Boston, San Francisco and Washington, D.C., and helped to develop a "white paper" of recommendations.

These recommendations include the need for a rescue vehicle that could bring sick or otherwise injured astronauts back to earth for treatment. "The best turnaround time possible with the four shuttle fleet right now is a wait of about 28 days between shuttles. And that's with everything working perfectly," according to Linder. "In actuality, it's probably closer to two months, so if somebody is really sick, that's a long time to wait."

Another suggestion made by Linder's study group was the development of a computer data base for the longitudinal study of all astronauts. Longitudinal studies would provide information about the long-term affects of the lack of gravity on the muscles and skeleton, which include the loss of calcium from the bones and atrophy of the muscles. Such studies will also likely address the affects of radiation exposure, space flight anemia and changes in white blood cells.

The group also recommended that there be a physician present on the space station at all times.

Would Linder himself like to be an astronaut? "What do you think?" he asks. Linder first applied to be an astronaut while he was in college, but could not qualify without a college degree. Although he's still trying to get into the space program, he admits that, without flying experience, his chances are slim. Linder may have a better chance of visiting space as a payload specialist—someone who is not full-time, but gets on to do some specific experiment.

"My first personal goal is to obtain a global view, to really see the whole earth and take it in, to appreciate it," he says. Linder was a winner of the National Space Society's Space Outreach project in 1985 for his essay, "A Global View Developed Through the Macroscopic of Space." In that essay, Linder outlined his vision for a meeting place in space, which would be used by international politicians, scientists, philosophers and civilians. "The vantage point of earth orbit would lead to a global awareness which would protect us from war, other forms of environmental destruction and potentially self-annihilation," he wrote. "On the one hand, a participant in this hotel-in-the-sky could look at the great expanses of darkness above and come to realize just how insignificant our planet is on a galactic scale. But, looking downward, he/she would see the beautiful blue globe of the Earth and note that there are no borders other than geological ones (as the Saudi Arabian Prince observed recently on a Shuttle flight). Taking an analogy from *The Lives of a Cell*, by Lewis Thomas, these people would come to appreciate our many nationalities and cultures as unique and important to maintain, just as a cell supports many different specialized organelles, but that we must work together to ensure our mutual survival. This I call a truly global view, obtained through the macroscopic of space, and it is one that must prosper if our only home, the Earth, is to continue to prosper."

Linder's other reason for wanting to be an astronaut is that it would be fun. "I'd like to help the U.S. space program because that is the future," he says. "Human nature has a sense of adventure to it. To just be satisfied, to sit back and not seek the unknown seems counter to the way human beings develop and society progresses." ■



Barry J. Linder, M.D.

THE ALUMNI REPORT

Doc for a Day

The first year of medical school, with its extensive booklearning and concentration in the basic sciences, can be a far cry from what most practicing physicians actually do. So when the Alumni-Freshman Visitation Program offered Tristan McGovern the chance to be "doc for a day," he took it.

As a participant in the Medical Center Alumni Association-sponsored program, McGovern was excused from classes for an entire afternoon to see patients with local rheumatologist Francisco J. Garriga, M.D. '70, at his office in Florissant.

For McGovern, who is a former marine, it was an opportunity "to get into the trenches and see where the rubber hits the road." Garriga, on the other hand, viewed the visit as a way to reinforce his own medical knowledge and perhaps learn something new by explaining it to someone else.

McGovern came into Garriga's office thinking that he wanted to be a surgeon, but discovered that his visit with Garriga expanded his horizons and may even have changed his career goals. He was especially struck by the "kingpin"-like role Garriga plays in the lives of his patients, many who require the services of surgeons, psychiatrists, therapists and other specialists. "He's right in the center, integrating all of this stuff," McGovern says of Garriga. "To see this guy at work was just wonderful."

As he followed Garriga from one patient to the next, McGovern encountered a whole host of ailments associated with chronic diseases such as arthritis, which cannot be cured, but require management.

In contrast with a surgeon, who gets immediate gratification from removing or repairing the source of suffering, an internist must often be content to simply alleviate the suffering so that his patients suffer as little as possible, according to McGovern, who recognized this as having a more subtle, yet perhaps deeper reward. "The big payoff is that his patients are grateful to him and really respect him for what he does for them," McGovern says of Garriga's job as an internist. "For many of them, he is their last hope."

Between patients, Garriga discussed how chronic pain affects people's lives, going beyond the obvious physical problem of not being able to button oneself up to the more important issues of how chronic pain affects patients' marriages, work, their entire lives.

McGovern's afternoon with Garriga not only strengthened the student's ulterior motive for going into medicine (to help people), but also reinforced things learned in his basic science courses. Having recently studied cholesterol and lipid transport in biochemistry, for example, McGovern saw patients with cholesterol deposits in their

carotid arteries. One lady came in with half of her face paralyzed due to the malfunctioning of a nerve McGovern had just learned about in his anatomy class.

Garriga and McGovern spent some time discussing the financial aspects of medicine, which Garriga has found to be a major concern among medical students today. Garriga described how he opened his practice 10 years ago, and how he runs

The most important business tip McGovern learned from Garriga, he learned through example. "It's a labor of love," he concludes. "You just don't work that hard for money."

Garriga truly loves the practice of medicine, which is why he is willing to share one or two afternoons each year with a young person who's also excited about being a doctor. "I've been doing it for four or five years



Francisco J. Garriga, M.D., (left) shows first-year student Tristan McGovern how to test for symptoms of arthritis.

it as a business today. He responded to McGovern's questions about physician oversupply and increased competition, by telling him that he will never find any profession as satisfying as medicine—regardless of the financial compensation—and that there's still plenty of room for outstanding doctors.

now," he says. "Anytime you teach, you learn a lot."

Alumni or students who would like more information about the Alumni-Freshman Visitation Program, would write or call the Medical Center Alumni Association at 660 S. Euclid, Campus Box 8049, St. Louis, MO 63110, 314-362-8277. ■

Conference Cancelled

The Medical Center Alumni Association-sponsored clinical conference, which was scheduled to be held in Hawaii during the month of February, has been cancelled due to small number of registrants. ■

Alum Estab- lishes Scholar- ships for Female Students

Female students at the School of Medicine can now receive additional financial aid through a special endowed fund for women, established by the late Cornelia Van Prooyen, M.D. '51.

Van Prooyen, who practiced internal medicine in Seattle Washington, bequeathed \$100,000 to the School of Medicine upon her death last April.

It was her wish that this money be used to help women students in the broadest sense, providing assistance for all legitimate fiscal needs, including child care. The first awards to women students will be made for the 1988-89 school year. ■



Paul Anderson, Ph.D., assistant professor of biomedical communication (left), Mabel Purkerson, M.D., associate professor of medicine, and Gerald Fischbach, M.D., Edison Professor of Neurobiology and head of anatomy and neurobiology, survey the new Nobel Laureate wall they helped plan for the National Institutes of Health centennial celebration. The permanent display of Nobel Prize winners with substantial ties to the university is located on the south wall of the McDonnell Sciences Building.

CLASS NOTES '30s and '40s

'10s and '20s

Marriott Morrison, MD. '19, is now a cited member of the American Academy of General Practice, after serving as a general practitioner for 50 years.

Milo K. Tedstrom, M.D. '24, was named the 1986 Physician of the Year in Orange County, California. He was also honored as Citizen of Leisure World in Laguna Hills last March.

Richard Sutter, M.D. '35, was recently named Medical Director Emeritus by the St. Louis Airport Authority for 17 years of outstanding service as Medical Director at Lambert-International Airport, and for his staunch support of commercial aviation in the St. Louis area.

Lloyd E. Rosenbaum, M.D. '37, retired in 1985. He is a member of the Indiana State Medical Association's 50 year club.

Joshua Jensen, M.D. '38, a retired surgeon and first chief on staff at Christian Hospital Northwest, is the 1987 recipient of the Hospital

Association of Metropolitan St. Louis's Andrew J. Signorelli, M.D. Award for enhancing cooperation, communication and effective working relationships between physicians and hospital administrators.

James Mann, M.D. '40, a semi-retired professor of psychiatry at Boston School of Medicine, writes that his son Jonathan, M.D. '73, is the director of a special AIDS program for the World Health Organization in Geneva, Switzerland.

H. Charles Franklin, M.D. '41, retired from his obstetrics and gynecology practice in Seattle, and has become a professional actor

on stage, movies and television. He was both a stand-in and photo double for actor Don Ameche in "Harry and the Hendersons," and is a principal performer in McDonald Restaurants' current commercial, *The New Kid*.

E. W. Busse, M.D., '42, Dean Emeritus of Duke University School of Medicine, has been named president of the North Carolina Institute of Medicine. He is also the recipient of the American Psychiatric Association's Warren Williams Special Award for 1987.

James H. Cravens, M.D. '43, was recently honored as the Dr. Albert Pisani Pediatrician of the Year for 1987. The annual award is granted by the Illinois Chapter of the American Academy of Pediatrics for dedicated service to medicine, to the community and to the health and well-being of the children of Illinois.

John Clough, M.D. '44, recently spent two summers as a physician volunteer in Denali National Park, Alaska and three months in Peshawar, Pakistan as an instructor at a school for Afghan medics.

Samuel B. Guze, M.D. '45, received the 1987 Achievement Award from the American Academy of Clinical Psychiatrists and a Distinguished Public Service Award from the Department of Health and Human Services for outstanding contributions to the understanding of genetic and environmental factors in the development of alcoholism.

Helmuth E. Hoff, M.D. '45, retired in July of 1986. He was re-certified in A.B.F.P. last July, and has been traveling extensively in the Eastern and Western United States, Canada, Europe and the Soviet Union. He is planning a South American trip for this March.

Joseph M. Natterson, M.D. '48, is writing a book called "Interpretation," which deals with intervention in psychoanalysis and analytic psychotherapy. Natterson practices psychiatry in the Los Angeles area, and teaches at the University of California at Santa Cruz and the University of Southern California.

Shirley Peterson, M.D. '49, of Barrington, Illinois, has retired after almost 40 years as a pediatrician. She is looking forward to devoting more of her time to growing flowers and cultivating her interest in birds and wildlife, and sprucing up her home.

'50s and '60s

James Benepe, M.D. '54, retired from the Veteran's Administration on his 60th birthday, and also retired from the Army Reserve. He's doing some consulting, but mostly golfing, shooting and fishing.

William D. Sawyer, M.D. '54, resigned as dean of Wright State University School of Medicine to become president-elect and director of the China Medical Board of New York, Inc. The private foundation supports medical education at medical colleges throughout the Far East.

Robert C. Drews, M.D. '55, received the Gold Medal of the Societe Opfalmologica Meridionale of Italy last May, and was recently awarded another gold medal from the University of Rome.

Doris Jasinski, M.D. '56, and **Cas Jasinski, M.D. '57**, retired from clinical practice, but still do limited consultations.

Lawrence C. Pakula, M.D. '57, was elected President of the Maryland Chapter of the American Academy of Pediatrics.

Richard A. Bohannon, M.D. '58, is the author of *Food for Life: The Cancer Prevention Cookbook*, published in 1986 by Contemporary Books, Inc. of Chicago. The soft cover edition was printed last September.

Tony Tathman, M.D. '64, chief of urology at St. Luke's Hospital in St. Louis, is the author of a children's book, *Tali the Christmas Star*.

John Hered, M.D. '67, is a clinical assistant professor of surgery at the University of Kansas School of Medicine in Wichita. He is on the neurosurgery staffs at St. Francis, St. Joseph and Wesley hospitals.

Arnold E. Katz, M.D. '67, was appointed professor of otolaryngology at Tufts University School of Medicine in Boston.

'70s and '80s

Toby Simon, M.D. '70, was named professor of pathology and director of the new transfusion medical center at University of New Mexico School of Medicine.

Thomas Clark Hill, M.D. '72, passed part II of the American Board of Emergency Medicine Certification Exams. He is now board certified in both emergency medicine and family practice.

S. Jenkins, M.D. '73, is current President of the Montgomery County Medical Society in Montgomery County, Texas.

Robert H. Karl, M.D. '73, and his wife Nilza live in Miami with their two children: David, 6, and Laura, 4. Karl is chief of cardiology at Baptist Hospital. He has climbed the Kilimanjaro and is a karate brown belt.

Roslyn Kaplan Yomtovian, M.D. '74, just accepted positions as director of the blood bank at University Hospitals of Cleveland and assistant professor of pathology at Case Western Reserve University.

Jacqueline Krohn, M.D. '76 and Roger Stutz are the proud parents of baby girl, Samantha, born last November.

Stuart R. Schlanger, M.D. '77, practices internal medicine in Omaha, Nebraska and the rural Missouri Valley. His hobby is physical fitness, participating in triathlons and serving as medical consultant to Triathlon Federation U.S.A. He finished second in his age group at the Annual Empire State

Building Run Up, climbing 86 floors, 1,575 steps.

Lionelle D. Wells, M.D. '77, was recently appointed co-director of labs at Medical Center Labs in Kankakee, Illinois. He also serves as an anatomic clinical pathologist at St. Mary's Hospital.

Nicholas B. Couper, M.D. '78, and his wife Elizabeth had their first child, Catherine Elizabeth, last August.

Allen J. Sedman, M.D. '78, has been promoted to vice president of clinical pharmacology in the Pharmaceutical Research Division at Parke-Davis.

Dale Anderson, M.D. '79, has been named medical director of Family and Personal Support Centers of Greater St. Louis, the only family service nationally to hold three major accreditations, including the Joint Commission for Accreditation of Hospitals.

Jeffrey P. Cichon, M.D. '79, and his wife Vicki just had their third child, Nicholas Peter, who along with Jamie Lee and Danielle Lynn are happy and well, living in the Las Vegas sunbelt with their parents. Cichon's orthopedic surgery practice is booming, and he was recently selected as a delegate-at-large to the Nevada State Medical Association. He was happy to hear about fellow classmates in the spring issue of *Outlook*.

Jack DiMarco, M.D. '79, is medical director of Our Lady of Lourdes Rehabilitation Center in Camden, New Jersey.

Gail Lowenstein, M.D. '79, is married and the mother of two children. She

is currently medical director of a 200 bed nursing home affiliated with Montefiore Hospital in the New York Bronx.

Cathy Jane Lazarus, M.D. '81, and her husband Eric Simon have one son—Stuart Alan. Lazarus is working full-time at the Washington University Student Health Service.

Raymond Phillips, M.D. '81, is completing a fellowship in gastroenterology at Walter Reed Army Medical Center. He and his wife Merian live in Silver Spring, Maryland with their two children, Rachel and Laura.

Myron Tanenbaum, M.D. '81, limits his practice in Miami, Florida to oculo-plastic surgery and diseases. He recently co-authored and co-edited the textbook, *Oculoplastic Surgery*, published in 1987 by Raven Press.

John Bellatti, M.D. '82, has joined the Hawaii-Permanent Medical Group as the orthopedic surgeon at their new Kona Office.

David J. Kraus, M.D. '82, finished his residency at Hahnemann University in Philadelphia last June. He is now a board-certified radiation oncologist at Greater Baltimore Medical Center in Baltimore, Maryland.

Eric Thompson, M.D. '82, completed his residency in general surgery at Mayo Graduate School of Medicine. He will begin his fellowship in cardiothoracic surgery at St. Luke's Hospital in Kansas City, Missouri.

Carol S. North, M.D. '83, published a book last year called *Welcome Silence*, which is about her battle with

schizophrenia. The book was selected by the Book of the Month Club and is also under option for a Hollywood movie. North, who joined the psychiatry faculty at the School of Medicine last July, has appeared on several television shows, including the "Today Show" and was featured in a November issue of *People* magazine.

Christina M. Parker, M.D. '83, is an immunology fellow at Childrens Hospital in Boston. She is married to Harry Braddock.

Michael Kastan, M.D. '84, is the father of a one-year-old son named Benjamin.

Susan Rollins, M.D. '84, is completing her pathology residency at the University of Utah and will begin a fellowship in surgical pathology at LDS hospital in Salt Lake City this July.

Steven Winman, M.D. '84, is a gastroenterology fellow at Yale. He was married to Terri Martin last September.

Robert Jarka, M.D. '85, and his wife enjoyed the birth of their first child, Nicholas Robert, born last April.

FORMER HOUSE STAFF NOTES

Israel Barken, M.D., F.H.S. in urology, was recently awarded a patent for a new method and apparatus for computer-controlled laser surgery that can be used in prostate gland removal and procedures with diseased coronary arteries.

Robert C. Cooke, M.D., F.H.S. in renal diseases, has moved to Memphis, Tennessee after serving for many years on the faculty at Johns Hopkins. He is now professor of medicine at the University of Tennessee and chief of nephrology at the Veteran's Administration Medical Center.

M. G. Fiorilli, F.H.S. in infectious diseases, completed a two-year term as chief of medicine at Halifax Memorial Hospital and as President of the Halifax/Northampton Counties Medical Society. He lives in Roanoke Rapids, North Carolina.

Charles P. Hughes, M.D., F.H.S. in neurology and neurological surgery, has been appointed medical director of Evergreen Manor, a Fort Oglethorpe nursing home recently developed by Greenleaf Health Systems Inc.

IN MEMORIAM

Wilma E. Baum, N.U. '41, formerly Wilma Earnst, died August 8, 1987.

Lee D. Cady, M.D. '22, died August 23, 1987.

Clifford C. Kane, M.D. '27, died October 3, 1987.

Mrs. George Lewis, N.U. '30, formerly Alta Ferne Drake, died July 18, 1987.

Benjamin G. Strehlman, M.D. '40, died September 15, 1987.

Barret L. Taussig, M.D. '32, died September 7, 1987.

Cornelia M. Van Prooyen, M.D. '51, died April 15, 1987.



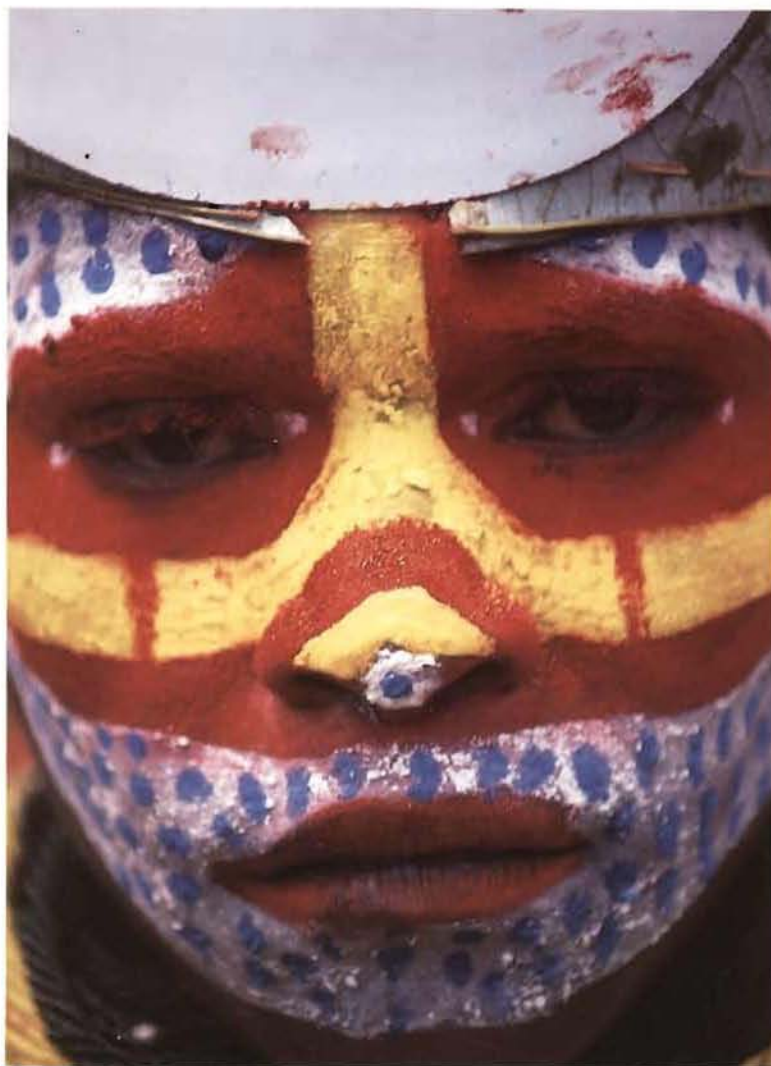
Photo by Charles Miller, M.D., shows Haitians selling hand-made flutes. Haiti was one of Miller's many stops in his travels to the Third World. See story on page 20.

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

AT WASHINGTON UNIVERSITY MEDICAL CENTER

660 SOUTH EUCLID AVENUE

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Dressed in native garb, this eastern highlander from Papua New Guinea was a costume contest competitor at the traditional Sing-Sing, a nationwide celebration held once every two years. Photo by Charles Miller, M.D. See "Physicians Abroad" story on page 20.
